TITLE OF CLINICAL RESEARCH STUDY

ADRN-13: A Pilot Study to Evaluate the Survival of Transplanted *Staphylococcus hominis* A9 on the Skin of Adults with Moderate-to-Severe Atopic Dermatitis

PRINCIPAL INVESTIGATOR

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YOUR PARTICIPATION IS VOLUNTARY

This study will be explained to you. You will have the opportunity to ask questions. Taking part in this study is up to you. If you sign this consent, you agree to take part in the research study. You may change your mind at any time. We will give you a copy of this signed consent form to keep.

CONSENT KEY INFORMATION:
The first pages of this document include a summary of the research study to help you decide whether or not to participate. Detailed information is provided after the key summary information.

Why is this research being done?

We would like to learn if a new therapy, a spray containing infection fighting bacteria, can improve symptoms of atopic dermatitis (AD) and would like to study how long the infection fighting bacteria will survive on the skin after application.

How long will this research last and what will I need to do?

Your participation in this study will last approximately 53 days.

If you agree to participate, you will complete a Screening Visit and the clinical staff will take your vitals and record your height and weight. They will ask you questions about your medical history and any medications or therapies you're currently using for your atopic dermatitis.

If you are not currently using any other medications or therapies, skin swab samples will be collected from both of your arms, and the clinical staff will give you a moisturizer to use on your arms for about **one week**.

If you are using other medications or therapies, you will be asked if you are willing to stop using the medications or therapies to continue in the study. Depending on the medication or therapy, you will need to stop use 7 to 28 days prior to the next study visit. **If you agree to stop,** you will be asked to return to the clinic after you are no longer using the medications or therapies, to have your skin swabs collected.

A few days later, you will be contacted regarding your swab results and eligibility to continue in the study. If eligible, you will be asked to return to the clinic for a Treatment Visit about 1 week after your skin swabs were collected. During the visit, skin swabs will be collected from your arms and face prior to receiving treatment. A member of the clinical staff will then apply the therapy spray to either your right or left arm

and a placebo spray (spray without the bacteria) to your other arm. You and your doctor will not know which spray is applied to each arm. You will be asked to remain in the clinic for about **6 hours**, to have additional skin swabs collected.

You will be asked to return to the clinic for up to 5 additional visits **(24 Hours, Day 3, Day 10, Day 17, Day 24)** following your Treatment Visit. During each visit, skin swabs will be collected from your face and arms. You will return to clinic for 24 Hour and Day 3 Visits. Based on the amount of bacteria still present on your skin after the Day 3 Visit and each subsequent visit, **you may be told you do not have to return for the Day 10, Day 17, and/or Day 24 Visits.** All participants will be asked to complete a Day 31 Final Phone Visit.

Is there any way being in this research can hurt me?

All of the study procedures that will be conducted on you have little to no risk, with one exception. The application of the new therapy has a small risk of skin infection. The likelihood of participants developing a skin infection is low.

The risks for you from the study procedures are discussed in detail in Section 3, "Risks and/or Discomforts."

Will being in this research study help me in any way?

There may or may not be a direct benefit to you from being in the study.

What other choices do I have besides taking part in this research?

You do not have to take part in this research study. You can still receive treatment for your atopic dermatitis at <Insert Site Name>.

DETAILED CONSENT INFORMATION

The rest of the consent document includes detailed information about this study.

1. INTRODUCTION/BACKGROUND

Atopic dermatitis, also called eczema, is a disease with dry, scaly, itchy skin. People with atopic dermatitis often experience complications of recurrent bacterial and viral skin infections. They experience recurring infections with a specific bacterium, *Staphylococcus aureus*, or Staph infections. The viruses, bacteria, and fungi, which cause the infections, interact with the immune system and trigger worsening of atopic dermatitis. This defect in the immune system's response creates a cycle of skin infection and worsening of atopic dermatitis. Standard treatment of bacterial infections includes antibiotics removing good and bad bacteria from the skin. Prolonged use of antibiotics also generates resistant bacteria, making the treatment ineffective.

2. STUDY COMPONENTS

This study is funded by the National Institute of Allergy and Infectious Diseases (NIAID).

This study will enroll approximately 20 participants, 18 to 80 years of age, from one center in the United States. All participants will have atopic dermatitis.

If you agree to participate in this study, you will be required to comply with UCSD's current institutional policies and procedures for COVID-19. These requirements will be communicated to you at the time of visit scheduling and prior to any scheduled appointments.

If you choose to participate in this study, you will have one dose of therapy with infection fighting bacteria applied to one of your arms and a placebo (product without the bacteria) applied to your other arm. You will not be able to choose which product is applied to each arm. Neither you nor your study doctor will know which product was applied to each arm. You will be randomly assigned, much like flipping a coin, to receive either the spray with bacteria or the placebo on your dominant arm.

Your participation in the study will last approximately 53 days and require 8-9 visits to <Insert Site Name>. If you are using medications/therapies at your first clinic visit, you may be asked to return for an additional clinic visit after you have stopped using the medications/therapies. The study doctor will review medications/therapies you are currently using to decide if they are safe to stop using while participating in the study. You must agree to stop using any prohibited medications/therapies while participating in the study.

If you are a female participant of reproductive potential and sexually active, you will be asked to use adequate contraception, over the course of your participation in the study. Acceptable methods of contraception for female participants include total abstinence, oral contraceptives, intrauterine device (IUD), barrier method with spermicide, surgically sterilized partner, Depo-Provera, Norplant, NuvaRing, or hormonal implants.

If you agree to participate in this study, you will be given Cetaphil lotion to use for about one week on your arms prior to confirming your eligibility to continue and receive the therapy product. After this, we would like you to use the Cetaphil lotion we will provide on your arms where we apply the treatment and on the area we swab on your face as needed for dry skin, for the duration of the study. We will also give you Dove moisturizing soap for use when showering over the course of your participation. You will not be permitted to use the Dove soap on your arms, and you will be asked to refrain from swimming in chlorinated pools/hot tubs through your last clinic visit. We will give you a handcard that summarizes all of these reminders.

The following procedures will occur during this study:

Screening Visit (Day -14 to Day -7)

Your initial visit to the center will take approximately 1.5 hours to complete. During the visit, the following will occur:

- **Consent: We will explain the study to you**. You will be given time to read this consent form and ask questions. Once all of your questions are answered, you will sign this consent form if you want to participate in the study.
  We may also talk to you over the phone about this study or send this informed consent document to you before you come into the clinic for an in-person visit. If you receive it before the clinic visit, please review the entire document. Do not sign and date the document until after we contact you to discuss the document. We may be able to discuss the consent by video or phone. If you agree to join the study, you can sign and date the document during our discussion. If you provide a signature by signing and dating with an actual pen, you will need to mail it back to us or bring it during your visit to the clinic. If you provide an electronic signature, we will give you instructions on how to return the form electronically.
- **Questionnaires:** You will answer some questions about your contact information and some questions to determine if you are eligible for this study. These questionnaires are not tests. There

are no right or wrong answers to the questions. If you do not understand certain questions, you may ask the study staff members for more information.

- **Physical Exam:** You will receive a physical exam by a study doctor or another qualified staff member. The purpose of the exam is to make sure that you meet the health requirements for the study. During the exam, a member of the study staff will ask you questions about your health and atopic dermatitis.
- **Medication/Therapy Review:** A member of the study staff will ask about the medications you have recently taken and any therapies you have used. The use of certain medications may mean that you will need to return for an additional visit to continue your participation.
- **Pregnancy Status and Test**: If you are a female participant and do not self-report as pregnant, you will be asked to give a small sample of urine for a pregnancy test. Results of the pregnancy test will be reported to you. If your pregnancy test is positive, you will not be allowed to participate in the study.
- **Vital Signs, Height, and Weight:** A member of the study staff will check your vital signs, (temperature, heart rate, respiration, and blood pressure), height, and weight.

At the end of the Screening Visit, if you meet all other eligibility requirements and have not taken or received certain medications and therapies for your atopic dermatitis, you may be able to complete your Pre-treatment Visit on the same day as the Screening Visit.

If you are currently using other medications or therapies, wish to continue participating in the study, and meet all other eligibility requirements, the study team will schedule your next study visit after you have stopped using the medications/therapies. The study doctor will review your specific medications/therapies and confirm the length of time you have to stop use before scheduling your next visit. This length of time could be up to 28 days or as short as 7 days.

If you do not meet all eligibility requirements or you are unable or unwilling to stop the use of certain medications/therapies, you will not be allowed to participate in the study.

Pre-treatment Visit (Day -7)

After the Screening Visit, if you are eligible, you will be asked to complete the Pre-treatment Visit. Based on your medication/therapy use, this visit may be on the same day as your Screening Visit or 1-2 weeks later. This visit will take about 1 hour if conducted on a different day than Screening and about 30 minutes if conducted on the same day. During the visit, the following will occur:

- Questionnaires
- Physical Exam
- Medication/Therapy Review
- Vital Signs
- Pregnancy Status (Female participants only)
- **Skin Swab Collection:** A member of the study staff will take pictures of your arms. A total of 8 swab samples will be collected from areas of affected and unaffected skin. The samples will be collected by rolling a sterile swab over the skin. Collection of each swab will take about one minute and is painless. Your skin swabs and pictures will be labeled with a number only, and not your name. The swabs will be used to look at bacteria growing on your skin.
- **Moisturizer Use:** The study team will give you a moisturizer to use at least twice a day on your arms for a total of about 7 days before your next visit.

A few days following your Pre-treatment Visit, a member of the study team will contact you about your swab results and eligibility to continue with study treatment. If your results meet eligibility for a group that has already enrolled enough participants, you may not be able to continue in the study.

Treatment Visit (Day 0)

Seven days after your Pre-treatment Visit, if you are eligible you will be asked to return to the clinic to have the therapy applied to one of your arms and placebo applied to the other. This visit will take approximately 7 hours. During the visit, the following will occur:

- Questionnaires
- Physical exam
- Medication/Therapy Review
- Pregnancy Test (Female participants only) and pregnancy status for partners of participants, as applicable
- Vital Signs
- **Skin Swab Collection**: 4 swabs will be collected from each arm, and 2 swabs will be collected from your face (10 swabs total)
- **Therapy Application:** A study staff member, while wearing gloves, will apply therapy spray to one of your arms and the placebo spray to your other arm.
- **Skin Swab Collection**: After therapy and placebo are applied to your arms, 8 swabs (4 from each arm) will be taken at each of the following time points: 15 minutes, 1, 2, 4, and 6 hours.

Follow-Up Visits (24 Hour and Days 3, 10, 17, and 24)

After the Treatment Visit, you will be asked to return to the clinic for up to 5 follow-up visits at 24 hours, and 3, 10, 17, and 24 days post treatment. Each visit will take approximately 45 minutes. During each visit, the following will occur:

- Physical Exam
- Medication/Therapy Review
- Pregnancy Status (Female participants and partners of participants, as applicable)
- Vital Signs
- **Skin Swab Collection**: 4 swabs from each arm and 2 swabs from your face will be collected at the 24 Hour Visit and Day 3 – 24 Visits

After the Day 3 Follow-Up Visit and each subsequent visit, the study staff will call you prior to your next scheduled visit if you do not need to return for the remaining follow-up visits (Day 10, Day 17, and/or Day 24).

End of Study Phone Visit (Day 31)

A study staff member will call you approximately one month after your 24 Hour Follow-Up Visit. The call will take approximately 15 minutes. You will be asked about your atopic dermatitis, any new symptoms you're experiencing, any medications/therapies you have used since your last visit, and whether or not you (female participants) or your partner have tested positive to a pregnancy test since your last visit to the center.

Unscheduled Visit

In the event you experience increased disease activity, signs and symptoms of an infection (pain or swelling at the site of treatment, fever, chills, or night sweats), or other concerns arise between your study visits, you may contact the clinical center. An emergency handcard summarizing these symptoms and the clinic phone numbers will be provided to you. Study staff will assess if you need to return to clinic for an additional visit. During the visit the following will occur:

- Physical Exam
- Medication/Therapy Review
- Pregnancy Status (Female participants and partners of participants, as applicable)
- Vital Signs
- **Skin Swab Collection**: total swabs collected will be at the discretion of the doctor

- **Blood Collection:** Approximately 0.5 teaspoon of blood may be collected from your arm to check your blood count. Additional blood, approximately 2 teaspoons per culture, may be collected at the discretion of the doctor. All of the blood can usually be collected with 1 needle stick. Your blood sample will be labeled with a number only, and not your name.

Should you experience increased disease activity or signs and symptoms of an infection and seek care at an outside facility, you should take the emergency handcard with you and provide it to the physician. The card will explain that you are in a clinical trial and include contact information for <Insert PI Name> and the 24 Hour On-Call physician at <Insert Site Name>. The card will also provide helpful information to the physician so he/she can treat your symptoms.

3. RISKS and/or DISCOMFORTS

Treatment and procedures in this research study may involve risks that are not possible to predict. You will be informed of any new risks that may be identified during the study. Below is a description of the risks we know about for each procedure. Please ask your study doctor or the research staff to explain any procedures or risks that you do not understand.

- **Questionnaires:** You may find that some of the questions are too personal. You may refuse to answer any questions that make you feel uncomfortable. There is also a possibility that your answers may be read by others outside of the study. Your name is not put on the questionnaires.
- **Physical Exam:** There are no known risks for the physical exam.
- **Medication/Therapy Washout:** Stopping medications and/or therapies prior to sample collection and during your study participation may cause worsening of your atopic dermatitis.
- **Pregnancy Test:** There are no known risks for the pregnancy test.
- **Vital Signs, Height, and Weight:** There are no known risks for having your vital signs, height, and weight checked.
- **Skin Swab Collection:** There are no known risks for the skin swab collection.
- **Therapy Spray Application:** Although the likelihood of participants developing a skin infection is low, a skin infection may occur where bacteria are applied to the skin. In order to reduce this risk, product will not be applied to your skin if you have evidence of skin cracks or breaks. Product will not be applied to your hands, and the study staff will wear gloves when applying the product, to reduce the chances of spreading bacteria onto other surfaces or people. If product is applied to other areas of the body, including eyes, nose, mouth, or genital area, there may be a higher risk of irritation or infection.
- **Blood Collection:** The risks of having blood taken may include pain, bleeding, or bruising. Some people may experience lightheadedness, nausea, or fainting. There is a potential for slight psychological stress from the procedure. If psychological stress is too much in the opinion of the participant or study staff, the procedures will be halted.
- There is a risk of loss of confidentiality of your information. Additional details regarding your confidentiality are included in Section 14. Confidentiality.

4. POTENTIAL BENEFITS

If you agree to take part in this study, there may be no direct medical benefit to you.
Information learned from this study may someday benefit the future treatment and care of people with atopic dermatitis.

5. ALTERNATIVES TO PARTICIPATION

There are other options available for you if you decide not to enroll in this study. You may receive treatment from a doctor without being in this study. You may choose to enroll in another study. You do not have to participate in this study in order to receive treatment at <Insert Site Name>.

6. NEW FINDINGS

The study doctor will tell you about any new information that may affect your willingness to continue in this study.

7. VOLUNTARY WITHDRAWAL FROM STUDY

You may decide not to take part or to leave the study at any time. If you decide not to participate or to leave the study, there is no penalty or loss of benefits in your routine medical care or any other benefit(s) that you would otherwise be entitled to receive.

If you leave the study prior to completion, we may ask you to complete a final assessment by phone, to confirm that any ongoing signs and symptoms related to your participation in the study are resolved and to answer any questions you may have about your atopic dermatitis.

If you decide to leave the study or if you decide you do not want us to keep your contact information, you can call <Insert Site Contact Number> to remove your information from our list. You can also write us at <Insert Site Address> to let us know that you want to leave the study.

8. REASONS WHY YOU MAY BE TAKEN OFF STUDY WITHOUT YOUR CONSENT

You may be removed from the study without your consent at any time. Reasons why you may be removed from the study include, but are not limited to, the following:

- The study doctor feels it is not in your best interest to continue in this study.
- You are unable to complete required study procedures, due to the development of a new disease, becoming pregnant, or starting treatment(s) not allowed for study participants.
- The study is stopped by <Insert Site Name>, the National Institute of Allergy and Infectious Diseases, or other health authorities.
- You do not comply with study procedures or follow study rules.

9. PREGNANCIES, BREASTFEEDING AND BIRTH CONTROL

You cannot participate in this study if:

- You are currently pregnant or breastfeeding.
- You plan to get pregnant in the next 2 months.

Treatments and procedures involved in this research project may involve unexpected risks to your unborn or nursing child. If you are female and of childbearing potential, a pregnancy test will be performed prior to your enrollment in this study.

If you are a female of child-bearing potential, you must agree to use birth control for the duration of your participation in the study. The acceptable methods of birth control are as outlined above in Section 2, Study Components.

If you are a female and become pregnant while participating in this study, or if you suspect that you have become pregnant, please contact < Insert PI Name> immediately.

10. COSTS TO THE SUBJECT (YOU)

There will be no charge to you or your health insurance company for any costs for the study therapy or placebo. There will be no charge to you or your health insurance company for any costs which are directly related to this study's procedures:

- Skin Swab Collection
- Blood draw

The normal costs related to your atopic dermatitis care during the course of the study will be up to you and/or your insurer:

- Physician visits outside of study visits
- Emergency room or urgent care visits
- Hospitalizations

11. PAYMENTS (REIMBURSEMENT)

You will be compensated for your time and effort to participate in this study.

At the Screening Visit, you will receive $40 for completing the activities, which include the questionnaires, pregnancy testing, and physical exam. If you complete the Pre-treatment Visit, you will receive an additional $50.

You will receive $150 for completing the Treatment Visit.

If you complete the 24 Hour, Day 3, Day 10, Day 17, and Day 24 Follow-Up visits, you will receive $50 per visit.

You will receive $10 for completing the End of Study Phone Visit.

In the event you are asked to return to clinic for an Unscheduled Visit, due to experiencing increased disease activity, showing signs and symptoms of an infection (pain, swelling, redness or tenderness at the site of treatment, fever, chills, or night sweats), or other concerns, you will receive $50 for each visit.

If you choose to or are asked to leave the study before it is finished, you will only be compensated for the activities you complete.

It is important to know that payment for participation in this study may be taxable income.

12. RESEARCH-RELATED INJURY

If you are injured or become ill because of taking part in this study, it is important to tell your study doctor < Insert PI Name>. Emergency medical treatment will be available to you, through <Insert Site Name>. You or your health insurance provider will be billed for the payment for any treatment you require as a result of a study-related injury. No other form of reimbursement is available. <Insert Site Name> and the National Institutes of Health, including the Division of Allergy, Immunology, and Transplantation do not have programs to pay if you are hurt or have other bad results that are not the fault of the study doctors. You may contact <Insert name of Research Staff Office> at <Insert Office Contact Number> for more information or to report study-related injuries.

In case of injury resulting from this study, you will not lose any legal rights by signing this form.

13. DISCLOSURE OF FINANCIAL CONFLICT OF INTEREST

Protocol Chair, Dr. Richard Gallo of the University of California – San Diego, is a co-founder of MatriSys Bioscience, Inc. (MatriSys) and has previously served as Chair of the company's Scientific Advisory Board. Dr. Gallo holds equity within the company and as Protocol Chair, Dr. Gallo helped design this study. MatriSys is working towards developing therapeutic products containing live bacteria to treat atopic dermatitis. MatriSys is not involved in the manufacture of the product to be used in this clinical study.

14. CONFIDENTIALITY

Your medical and research records will be confidential to the extent permitted by law. Efforts will be made to keep your personal information private. However, we cannot guarantee complete confidentiality.

You will be identified by a code, and personal information from your records will not be released without your written permission. You will not be identified in any publication or in the sharing of your data about this study. After the study is completed, the data may be placed in a central storage location. These data will not include your name or other information that can identify you. The purpose is to make study data available to other researchers. Information from this study may be put into databases along with information from other studies. There are different kinds of databases; some are publicly accessible, and some are restricted. Anyone on the internet can access publicly accessible databases. Only researchers who apply and are approved can access restricted databases. Traditionally used identifying information about you (such as name, phone number, address) will NOT be included or shared with others.

As an NIH funded study, you are further protected through a policy that prevents the study doctor from releasing any sensitive information about you that may identify you. This does not prevent you or a family member from voluntarily releasing information about this research.

Organizations that may look at and/or. copy your medical records for research, quality assurance, and data analysis include:

1. The National Institute of Allergy and Infectious Diseases (NIAID) sponsor of the research
2. NIAID representatives, agents, employees, contractors, and other persons assisting in conducting, monitoring or analyzing the study. This includes the study monitors from Rho, Inc., <Insert local IRB >, Principal Investigator, and research staff at <Insert Site Name>
3. The U.S. Food and Drug Administration
4. Other State and Local health authorities

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

15. PROBLEMS OR QUESTIONS

I can call …	At …	If I have questions or concerns about
During *<Insert Regular Clinic Hours>* *<Insert PI Name>* **Principal Investigator**	**Phone**: *<Insert Phone>* **Pager**: *<Insert Pager>* **Beeper #**	**General questions about the study** **Research- related injuries or emergencies** **Any research-related concerns or complaints** **Symptoms in between my regular scheduled study visits**
Outside of Regular Clinic Hours **On Call Physician**	**Phone**: *<Insert Phone>* **Pager**: *<Insert Pager>* **Beeper #**	**Research- related injuries or emergencies** **Any research-related concerns or complaints** **Symptoms in between my regular scheduled study visits**
<Insert Research Staff Office Number>	**Phone**: *<Insert Phone>* **Pager**: *<Insert Pager>* **Beeper #**	**General questions about the study** **Research- related injuries or emergencies** **Any research-related concerns or complaints**
<Insert IRB>	**Phone:** *<Insert Phone>*	**Rights of a research subject** **Any research-related concerns or complaints** **If investigator/study contact cannot be reached** **If I want to speak with someone other than the Investigator, study contact, or research staff**

16. FUTURE USE OF YOUR DATA/BIOLOGIC MATERIALS

Information about you, including your biospecimens, collected for this study may be shared with other researchers. It may also be used for other research studies. We will make sure that your identity cannot be linked to the information we share; your data and biospecimens will be coded so that other investigators will not have access to your personal information. We will not ask you for additional permission before sharing the information.

We are asking your permission to store unused skin swab samples and secondary samples created from your skin swabs collected during the course of this study to be used in the future for tests that aren't yet planned. No human DNA analysis will be performed on these samples.

The results of tests performed on stored samples or reports resulting from the analysis of your samples will not be given to you or your doctor, and they will not be put in your medical record. They will not identify you and will not affect your routine medical care.

There is no benefit to you from the storage of samples and information. The purpose of storage and sharing data is to make information available for use in health research and to share what is stored with other researchers. Collecting, storing, and sharing information and making it available for other studies may help people in the future**. Coded information** put into databases together with other stored information from many studies conducted in different places allow researchers to study the combined information and learn even more about health and many different diseases.

Samples will be stored at the University of California – San Diego. If you decide to allow storage, your samples and information may be stored for an unknown length of time.

Although your stored research samples will not be sold, the information obtained from the research performed on your samples may in the future lead to the development of commercial products. You will not receive any money from research using your stored samples and information.

There may be unknown risks associated with the storage and analysis of samples or the information resulting from the analysis of your samples.

You can change your mind at any time and ask to have your samples destroyed. This request should be made in writing to the study doctor. If you make this request, all remaining stored samples will be destroyed. However, the results of any previous tests using your stored samples will be used. Your decision regarding the storage of samples or the information resulting from the analysis of your samples will not affect your ability to participate in this study.

I agree to the storage and sharing of skin swabs or any secondary samples created from skin swabs and information resulting from the analysis of my samples for <u>other</u> tests not currently planned.

☐ **Yes** ☐ **No**

_____
Initials of Research Subject

17. PARTICIPANT SIGNATURE PAGE

Please sign below if you agree to take part in this study.

- **You have read the informed consent and had it explained to you**
- **You were given the opportunity to ask questions about the information**
- **You understand the risks and benefits of this study as explained in this consent form**
- **You voluntarily agree to take part in the study**

_____	_____	_____
Research Participant's Name *(Typed or printed)*	**Research Participant's Signature**	**Date**

Signature of person explaining and obtaining the consent:

_____	_____	_____
Name and Title *(Typed or printed)*	**Signature**	**Date**

(NOTE: This consent form with the original signatures MUST be retained on file by the principal investigator. A copy must be given to the research participant. A copy should be placed in the research participant's medical record, if applicable.)