Protocol:
CYN13-PicoRevlite

PICOSURE Alexandrite Laser AND REVLITE Nd:Yag Laser FOR THE TREATMENT OF UNWANTED TATTOOS

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FOR THE TREATMENT OF UNWANTED TATTOOS

PROTOCOL #: CYN13-PICOREVLITE

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INVESTIGATOR AGREEMENT

I have read the foregoing protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study as outlined herein and will complete the study within the time designated.

I will comply with Good Clinical Practice (GCP) regulations and guidelines during the conduct of this study.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the laser and the conduct of the study.

I further agree that Cynosure, Inc. or their designees shall have access to any source documents from which case report form information may have been generated.

_____ _____

Investigator's Signature Date

_____

Name of Investigator (Typed or Printed)

_____

_____

_____

Address of Investigator (Typed or Printed)

Protocol Number: CYN13-PICOREV

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1. PURPOSE AND OBJECTIVES

This is a prospective study to evaluate the PICOSURE Laser System for the treatment of unwanted tattoos.
Objectives:

1. Establish Treatment parameters
2. Compare to Revlite Laser System
3. To assess safety through recording of side effects during course of study.

2. BACKGROUND

Lasers are accepted devices for the removal of unwanted tattoos. Currently, Q switched Alexandrite and Nd:YAG lasers emitting wavelengths of 1064nm, 755nm and 532nm, are routinely used in the removal of unwanted tattoos. The lasers' Q-switched mode of operation allows the delivery of short (nanosecond) pulses that can disrupt or shatter the tattoo ink or pigment which is subsequently cleared by the body's own cells, the phagocytes or macrophages.

Tattoo removal often requires a series of treatments performed approximately every 6 weeks. Tattoos may be removed in as few as 2-4 treatments, but others may require six to ten, or even as many as twenty treatments to achieve clearance. Unfortunately, not all tattoos can be removed completely.

3. DEVICE DESCRIPTION

The RevLite Q-Switched Nd:YAG is cleared under FDA K083899 for Tattoo Removal.
The PICOSURE laser has been cleared by the FDA under 510 (k) K121346 for the removal of tattoos and benign pigmented lesions. It is believed that these shorter pulses may be more efficient in disrupting pigment and possibly resulting in better treatment outcomes.

The sponsor deems this device a non significant risk. The system was tested to ensure compliance with federal laser performance standards, 21CRF Part 1040.

See section 11 for full specifications.

4. SUBJECT POPULATION AND SELECTION CRITERIA

The study subject population will consist of up to 100 subjects. Up to 10 subjects will be receiving split tattoo treatments with the Revlite and/or the Pico Laser. The subjects will meet the selection criteria described as follows:

4.1 Inclusion Criteria

1. Is a healthy male or female between 18 and 65 years old.
2. Is willing to consent to participate in the study.
3. Is willing to comply with all requirements of the study including being photographed, following post treatment care and attending all treatment and follow up visits.

4.2 Exclusion Criteria:

1. The subject is female and pregnant, has been pregnant within the last 3 months, is currently breast feeding or planning a pregnancy during the study period.
2. The subject is hypersensitive to light exposure OR takes photo sensitizing medication.
3. The subject has active or localized systemic infections.

4. The subject has a coagulation disorder or is currently using anti-coagulation medication (including but not limited to heavy aspirin therapy {greater than 81 mg per day}).
5. The subject has any condition which, in the investigator's opinion, would make it unsafe for the subject to participate in this research study.
6. The subject is currently enrolled in an investigational drug or device trial, or has received an investigational drug or been treated with an investigational device within 3 months prior to entering this study.
7. The subject has used Accutane within 6 months prior to enrollment.
8. The subject has the need to be exposed to artificial tanning devices or excessive sunlight during the trial.
9. The subject has had prior treatment with parenteral gold therapy (gold sodium thiomalate).
10. The subject has a history of keloid scar formation.
11. The subject has evidence of compromised wound healing.
12. The subject has a history of basal cell carcinoma, squamous cell carcinoma or melanoma.
13. The subject has a history of immunosuppression/immune deficiency disorders (including HIV infection or AIDS) or use of immunosuppressive medications or has an autoimmune disorder.14. The subject has red tattoo ink allergy

5. STUDY DESIGN

Subjects will receive up to 10 laser treatments on their unwanted tattoo. The study subjects will return to the investigator site for follow-up evaluations. See section 5.4 for schedule and visit details.

5.1 Subject Assignment

All potential subjects will undergo a pre-screening interview where their medical history will be reviewed and inclusion/exclusion criteria verified. Subjects meeting the criteria for enrollment in the study will sign the informed consent form and be assigned a subject identification number. Subject identification numbers will be generated chronologically and assigned only to subjects who have met all inclusion/exclusion criteria and signed the informed consent form. Subjects will be de-identified through their subject identification number, which will be stored in a secure location.

5.2 Screening

- Consent must be signed.
- Medical history of each subject will be reviewed and inclusion/exclusion criteria verified. A limited physical exam (no pelvic and no rectal exam).
- Subjects meeting the criteria for enrollment in the study will sign the informed consent form and be assigned a subject identification number.

5.3 Laser Treatment

5.3.1 Pre-Treatment

- Photographs will be taken of the treatment area(s).
- Female subjects will be asked if they are pregnant and the date of their last menstrual cycle (no pregnancy testing will be conducted).

5.3.2 Procedure

- All laser operators and subjects will wear protective eye glasses during the laser treatments
- Subjects will receive up to 10 treatments, administered every 4-12 weeks.
- Adjunctive tissue cooling with chilled air (Zimmer Cooler) will be used during and/or after treatment to enhance comfort. If subjects require additional means of reducing treatment or post-treatment discomfort, an optional application of topical anesthesia, such as EMLA® , ElaMax® or BLT cream for up to 60 minutes prior to treatment may be used at the discretion of the Investigator.

5.3.3 Technique

- The appropriate parameters including the number of pulses will be determined by the physician.
- The laser hand piece distance gauge tip will be in contact with the skin.

5.3.4 Post Treatment

- Standard post-op wound care instructions will be reviewed.
- Aquaphor will be applied to the treatment and it will be covered with a non stick pad. The subjects will be instructed to change the pad twice per day for one week.
- Subjects may resume normal activities after treatment.
- If treatment area is in a location that is exposed to the sun, the treatment area should remain covered at all times. If this is not possible, sun block with a broad spectrum UVA, UVB sunscreen of SPF 30 or higher should be applied to the treated area every 2 hours when exposed to sun and, and should apply protection throughout the study.
- This information is also included in the Informed Consent Form.

5.3.5 Unscheduled Visits

An unscheduled visit may be performed at any time during the study at the subject's request or as deemed necessary by the site Investigator. The date and reason for the unscheduled visit will be recorded in the source documentation.

5.4 Subject visit Schedule

- Visits will be required per schedule below:

Procedure	Screening /Baseline	Treatment 1-10 (every 4-12 weeks)	2 Month Follow Up (+/- 1 Month)
Consent	X		
Medical History	X		
Photos	X	X	X
Treatment		X	
Events Assessment	X	X	X
Satisfaction Questionnaire (Subject and PI)			X

The sponsor anticipates that all subjects can be enrolled within 2 months. Treatment and follow-up on the last subject entered into the study will add at least another 12 months to the study duration. Subject participation in the study is expected to last up to 13 months. The total study duration is anticipated to last a total of 15 months.

5.5 Pregnancy

Females may not participate in this study if they are pregnant, breastfeeding, were pregnant within the last three months or are planning a pregnancy during the course of the study. Date of last menstrual cycle will be recorded.

If the subject thinks they have become pregnant during the study it is important that they inform the study doctor immediately. If she becomes pregnant or thinks that she may be pregnant, she will be removed from the study and will ask to perform a final evaluation. The study doctor should refer her to seek obstetric care, the cost of which will be her responsibility. The study doctor may request to track the pregnancy and will report the pregnancy to the Sponsor and the IRB.

5.5 Right to Withdraw or Removal from Study

The subject is free to withdraw from this study at any time. The subject must inform the Investigator immediately if they intend to withdraw. To terminate the subject's participation in this study, they must contact the study doctor at the contact information listed on page one of the informed consent form. They will be asked to come to the study clinic or doctor's office to complete some end of study procedures which are listed in the Withdrawal Procedures section of the informed consent form. Their decision to participate in this study or to withdraw from this study will not influence the availability of their future medical care and will involve no penalty or loss of benefits to which they are otherwise entitled.

The Investigator in charge of the study can remove the subject from this study without their consent for any reason, including, but not limited to:

a. His/her judgment that any condition or circumstance may jeopardize their welfare or the integrity of the study.
b. Their failure to follow the instructions of the investigator(s).
c. If the study is stopped by the sponsor and/or doctors participating in the study prior to completion.

5.6 Photography

Photos will be taken with an appropriate high resolution digital camera. It is important to record and carefully reproduce the camera settings (lighting, distance from the treatment area, background, polarization, etc.) at each visit, so that photos are suitable for comparison. If the subject does not wish to have their photos taken, they cannot be in the study.

5.7 Evaluation Methods

5.7.1 Tattoo Clearance

A photographic Scale will be used to evaluate outcomes. Blinded evaluators will grade the tattoo clearance of photographs taken of the subjects at baseline and post treatment. The results will be compared to determine improvement.

5.7.2 Investigator and Subject Questionnaires:

Questionnaires will be used to assess Investigator and Subject satisfaction at the 2 month follow up visit with their cosmetic results when compared to baseline photos using a six point scale ranging from “extremely satisfied” to “extremely dissatisfied”.

5.7.3 Events

Recording of events will take place at all visits.

6. RISK MANAGEMENT

The investigator in this clinical trial has been invited to participate based on his previous experience with the use of laser systems in dermatology. Experience with laser treatments is the most critical element in managing subject risk in this trial. Additionally, all laser operators and subjects will wear protective eye glasses during the laser treatments. All other known risks will be disclosed to the subject via the informed consent process. Since this is an elective procedure and the subjects are volunteers, it can be assumed that their signature on the informed consent is indicative of their agreement to accept the risks involved.

7. ADVERSE REACTIONS

Side effects means anticipated reactions to treatment and typically resolve spontaneously. Anticipated events means reactions to treatment previously observed that may require medical intervention but are not serious in nature.

All adverse events that occur, starting from the time of the first treatment will be recorded in the Source Documents.

Adverse Events occurring will be captured and followed until the condition resolves, stabilizes, or is otherwise explained, or the subject is lost to follow-up. Subjects will be instructed that they may contact the Principal Investigator at any time throughout the course of the study.

The Investigator will review each event and assess its relationship to the laser treatments (not related, unlikely, possible, probable, and highly probable). The following definitions will be used for rating relationship to the laser treatments:

- Not related – The event is clearly related to other factors such as the subject’s clinical state, therapeutic interventions, or concomitant medications administered to the subject.
- Unlikely – The event was most likely produced by other factors such as the subject’s clinical state, therapeutic interventions, or a concomitant medication administered to the subject; and does not follow a known response pattern to the investigational product.
- Possible – The event follows a reasonable temporal sequence from the time of investigational product administration; and/or follows a known response pattern to the study sampling sessions; but could have been produced by other factors such as the subject’s clinical state, therapeutic interventions, or concomitant medications administered to the subject.
- Probable – The event follows a reasonable temporal sequence from the time of investigational product administration; and follows a known response pattern to the investigational product; and cannot be reasonably explained by other factors such as the subject’s clinical state, therapeutic interventions, or concomitant medications administered to the subject.
- Highly Probable – The event follows a reasonable temporal sequence from the time of investigational product administration; and follows a known response pattern to the investigational product; and cannot be reasonably explained by other factors such as the

subject's clinical state, therapeutic interventions, or concomitant medications administered to the subject; and either occurs immediately following investigational product administration, or improves on stopping the investigational product, or reappears on repeat exposure, or there is a positive reaction at the application site.

Each adverse event reported will be graded on a 3-point severity.

The following definitions for rating severity will be used:

- Mild – easily tolerated, causing minimal discomfort, and not interfering with normal everyday activities.
- Moderate – sufficiently discomforting to interfere with normal everyday activities.
- Severe – incapacitating and/or preventing normal everyday activities.

A Serious Adverse Event is any adverse device experience that results in any of the following outcomes: death, a life-threatening adverse device experience, in-patient hospitalization or prolongation of hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may or may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse device experience when, based upon appropriate medical judgment, they may jeopardize the subject or subject may require medical or surgical intervention to prevent one of the outcomes listed in this definition

If any of the above adverse events are serious as defined by the FDA Code of Federal Regulations (CFR), Title 21, special procedures will be followed. All serious adverse events will be reported within 24 hours of acknowledgment to the Medical Monitor whether or not the serious events are deemed sampling session-related. All serious event reporting will adhere to 21 CFR part 812 and the IRB will be notified accordingly.

The Medical Monitor will enter the SAE information into the database and submit a desk copy of the complete SAE report to the files.

Adverse events, whether serious or non-serious, will be followed until the condition is resolved, stabilized, or otherwise explained, or the subject is lost to follow-up. Adverse events will be captured up to one week after a subject completes the study and where appropriate, medical tests and examinations will be performed to document the resolution of event(s). Outcomes may be classified as resolved, improved, unchanged, worse, fatal, or unknown (lost to follow-up). Following the resolution of any study-associated adverse events there will be no further adverse event reports for that subject.

PICOSURE/REVLITE
Risks to the subjects who participate in this study are the same as those for the subject undergoing infrared laser treatment. Eye injury due to direct ocular laser exposure requires the use of protective eyewear. with an optical density of 755nm- ≥ 7.0 OD,532nm-≥ 7 OD, 1064nm ≥ 7OD.

Side effects of the laser treatment can include; Pain, blister, redness, swelling, bruising, pin point bleeding, crusting, itching, Some anticipated events from the treatment may include; infection, , allergic reaction, scarring, burn, hypopigmentation and hyperpigmentation.

Proper pre and post treatment standards and wound care reduces the risk of these

complications; however these conditions may or may not resolve over time.

Incomplete removal is relatively common,

Sunburn may occur if subject has unprotected exposure to ultraviolet (UV) light.

8. PROTOCOL DEVIATIONS

All requests for protocol deviations by the Investigator have to be communicated to the sponsor in writing and if accepted by the Sponsor must be approved by the IRB. If a deviation occurs, the Investigator must inform the Sponsor and IRB in writing within 10 days.

9. DATA COLLECTION AND MONITORING

The sponsor will train the site and be present at initiation of treatment. The sponsor will also monitor the site at various intervals and upon request expects to receive intermediate results by fax following each visit to evaluate treatment progress. Case Report Forms and Investigator Binders will be reviewed for current data. The sponsor will collect data at the end of the follow up period. The sponsor will list the study on clinicaltrials.gov as required by FDA regulations.

10. CONFIDENTIALITY AND DISCLOSURE OF MEDICAL INFORMATION

As part of this study the Investigator and the team at the research facility will keep records of subject participation in the study. These study records will include personal information that the subjects provide including age, sex, etc., the results of the study, information about response to treatments, photographs taken during the study and other medical information relating to participation in the study.

Under federal law the study records cannot be used or disclosed by the research Investigator for research purposes unless subjects sign the informed consent authorization.

Some or all of the test results, photographs and other information will be reported to Cynosure, Inc. the manufacturer of the test device, and consultants that are helping conduct the study. The sponsor and its consultants will analyze and evaluate these results and information and may report them to the U.S. Food and Drug Administration (the FDA) or other regulatory agencies in the United States and/or foreign countries. Study records will be assigned a code number by the study team and the subject will ordinarily not be identified by name in the study records that are sent to the Sponsor and its consultants. However, The Sponsor and its consultants will have the right to see the complete study records.

The research facility will review and use the study records only for purposes of this study. They will keep the subject identity confidential and, except for the disclosures described above, will not disclose the study records to other parties unless disclosure is required by law. Once the research facility discloses information in the study records, photographs or medical records to the Sponsor or its consultants, the information will no longer be protected by federal law. Because of the need to release information to these parties, absolute confidentiality can not be guaranteed. However, the Sponsor and its consultants will only use the information for purposes of the study and will not disclose the study records to parties other than the FDA and similar government agencies, unless disclosure is required by law. If reports or articles are written about the study, you will not be identified by name in them. The study records may be retained at the research facility indefinitely following the completion of the study.

11. DEVICE SPECIFICATIONS

The Pico Laser is manufactured by Cynosure Inc.

Device Type	Alexandrite Laser
Wavelength	755nm, 532nm, 1064nm
Pulse width	0.5 - 0.8ns
Fluence	0.5 - 6*J/cm²*
Spot Size	2 –10mm

The Revlite Laser is manufactured by Conbio, a Cynosure company.

System Type	Nd:YAG
Wavelength	1064nm, 532nm
Pulse Width	5-20ns
Spot Size	1.2-8mm
Fluence	1.5 – 21 J/cm^2

12. LABELING

Sample labeling and directions for use are contained in the Operation Manual for this device.

13. CLINICAL RESEARCH CONDUCT

The study will be conducted in accordance with the protocol, International Conference on Harmonization (ICH) GCP guidelines, applicable regulations and guidelines governing clinical study conduct and ethical principles that have their origin in the Declaration of Helsinki. The investigator must ensure that the study is conducted in accordance with the provisions as stated in the FDA regulations and complies with the applicable local or regional regulatory requirements.

14. INFORMED CONSENT

During the screening, the investigator or a representative on their behalf will perform the informed consent process. At the screening, all aspects of the study will be discussed with the subject. A signed informed consent form (ICF) shall be obtained from the subject, clearly indicating his/her understanding of the study requirements, as well as the possible risks involved with study participation.

15. DATA ANALYSIS

In order to meet the objectives of our clinical study we will analyze tattoo clearance scores, PI and Subject satisfaction, and events.

16. REPORTING FOR THE STUDY

A study summary report will be generated. It will include a description of the clinical conduct of the study and results, and the statistical analysis described in the data analysis section of this protocol.

17. DISCLOSURE

The Principal Investigator, Medical Monitor, sponsor representative, and Cynosure employees have signed confidentiality agreements with the sponsor. This confidentiality agreement ensures that all information provided to the Investigator or Data Management and Statistics group dealing with the study and information obtained during the course of the study will be regarded as confidential.

18. RESPONSIBILITY OF THE INVESTIGATOR

The Investigator is responsible for ensuring that the clinical study is performed in accordance with the Declaration of Helsinki (revised version of Edinburgh, Scotland, 2000 including notes of clarification, Washington, 2002 and Tokyo, 2004) and FDA Good Clinical Practice Regulations (21 CFR parts 50, 56, and 812). Investigators will supply information to the sponsor such that the sponsor can comply with the Financial Disclosure Rules (21 CFR part 54).

19. PROCEDURE FOR AMMENDMENTS TO THE PROTOCOL

No deviations from this protocol will be permitted, except in a medical emergency, without the approval of the Sponsor. Any amendment to this study will be discussed by the Investigator and the Sponsor. If agreement is reached concerning the need for modification, this will be made in a formal amendment to the protocol. All revisions and/or amendments to the protocol must be approved in writing by the appropriate Institutional Review Board.

20. INSTITUTIONAL REVIEW BOARD

This protocol, informed consent forms, and any amendments to the protocol will be reviewed by the appropriate Institutional Review Board prior to initiation. The study will not be initiated without the approval from the Institutional Review Board.

21. TERMINATION OF STUDY

The Sponsor reserves the right to discontinue this study for administrative reasons at any time. The Investigator reserves the right to discontinue the study for safety reasons at any time in collaboration with the Sponsor.

22. STUDY RECORDS

All records and documents pertaining to the study will be maintained in appropriate permanent files as per the ICH guidelines for Essential Documents for the Conduct of a Clinical Trial and 21 CFR 11, and will be available for inspection by the Sponsor, Sponsor designee, or the Food and Drug Administration at any time.

23. CONFIDENTIALITY

After the informed consent has been signed, each subject will be entered on a screening/enrollment log, which will be kept with the study records. Once a subject is consented, a unique subject identification number will be assigned. No two subjects will have the same subject identification number. This subject identification number will identify the subject throughout the study and will be used for all source documents, and Data Collection Forms. The subject identification number will be held confidential so far as permitted by law. Investigative site staff, the Sponsor or its designee, and, under certain circumstances, the FDA and Institutional Review Board (IRB) will be able to inspect and have access to the subject identification number and the confidential data that it links to. Any publication or presentation of data will not contain any identifiable subject information.

24. DATA SECURITY

To ensure the privacy and confidentiality of data for this protocol, the data will be stored on a restricted access location on a company server. Access to the project directory containing the data will be limited to the investigators and research staff. Information about data security awareness is promoted through user training and education, supplemented by policies and procedures. Password protection will be used for all transactions that allow viewing, editing, and analysis of data, or that provide access to data fields derived from the original source documents.