A PRospective OpEn-Label Study usIng the RhinAer® ProcEdure for Treatment of Subjects SuFfering with Chronic Rhinitis - RELIEF

Protocol Number:	CTP1056
Protocol Date:	27 January 2021
Version:	C
Principal Investigators:	Jivianne Lee, MD UCLA Santa Monica Head and Neck Surgery 1131 Wilshire Blvd, Suite 302 Santa Monica, California 90401 Phone: 424-259-6559 email:jivianne@gmail.com
Sponsor:	Aerin Medical, Inc. 232 E. Caribbean Drive Sunnyvale, CA 94089 Contact: Anais Laborde Director of Clinical Affairs Phone: 650-518-9624 email: alaborde@aerinmedical.com
Sponsor Representative:	*<If the sponsor is not a resident in the country(ies) in which the clinical investigation is to be carried out, the name and address of a representative in that country (those countries) can be required according to national or regional regulations>*

INVESTIGATOR

I, the undersigned, certify that I have reviewed this Clinical Investigational Plan and agree to abide by the terms of the study described herein and within the Investigator Agreement, Clinical Trial Agreement and according to the Declaration of Helsinki and The Belmont Report as well as any conditions imposed by the reviewing Institutional Review Board, Ethics Committee, United States Food and Drug Administration or other regulatory agency.

Site Name: _____

Print Name: _____

Signature: _____ Date: _____

Table of Contents

Protocol Summary

Title of Study:	A P**R**ospective Op**E**n-Label Mu**L**ticenter Study us**I**ng the RhinAer® Proc**E**dure for Treatment of Subjects Su**F**fering with Chronic Rhinitis - RELIEF
Purpose:	The purpose of this study is to assess the clinical use of the RhinAer Stylus to treat tissue in the posterior nasal nerve area to improve symptoms in adults diagnosed with chronic rhinitis.
Indications for Use (United States):	The RhinAer Stylus is indicated for use in otorhinolaryngology (ENT) surgery for the destruction of soft tissue in the nasal airway, including in posterior nasal nerve regions in patients with chronic rhinitis. The Aerin Console is an electrosurgical system intended to generate radiofrequency electrical current for the use of an Aerin Medical Stylus. The Aerin Console is indicated for use in small clinic, office or hospital environments.
Intended and Indications for Use (European Union):	The RhinAer Stylus is intended to improve nasal breathing by modifying the soft tissues of the nasal airway. It is indicated for use in otorhinolaryngology (ENT) surgery for the destruction of soft tissue in the nasal airway, including in posterior nasal nerve regions in patients with chronic rhinitis. Device has CE Marking in EU. The Aerin Console is an electrosurgical system intended to generate radiofrequency (RF) electrical current for modification of soft tissues during ear, nose and throat procedures, when used with an Aerin Medical Stylus. It is indicated for use in delivering radio-frequency energy to tissues as part of ear, nose and throat procedures in small clinic, office or hospital environments.
RhinAer Treatment:	The RhinAer procedure will be performed in the study clinic using the RhinAer Stylus and Aerin Console. The RhinAer Stylus is a disposable handheld device capable of delivering bipolar radiofrequency energy to tissue when connected to the Aerin Console radiofrequency generating device. Participants will have both nostrils treated in the portion of the nasal cavity mucosa overlying the region of the posterior nasal nerve (the posterior middle meatus and posterior inferior meatus) during a single study procedure session. Each nasal cavity will be treated at 1, 2, 3, 4, or 5 nonoverlapping positions depending on the size of the target treatment area. Treatment settings to be used are temperature 60° C, power 4 watts, treatment time 12 seconds, and cooling time 0 seconds.
Study Design:	The study is designed as a multicenter (up to 20 sites), prospective, open-label, single-arm study.

	All participants will be evaluated prior to treatment and following treatment at week 13 (3 months). The 3-month evaluation will be used for the primary endpoint analysis. The study will have an extended follow-up phase with evaluations conducted at 26 weeks (6 months), 52 weeks (12 months), 104 weeks (24 months) and 156 weeks (36 months) to provide additional information on longer-term efficacy and duration of treatment effect.
Study Objective:	The primary objective is to assess the performance of the RhinAer procedure with respect to mean change in the 24-hour reflective Total Nasal Symptom Score (rTNSS) at 3 months posttreatment when used as a treatment for chronic rhinitis. A secondary objective is the evaluation of treatment effect duration through an extended follow-up to 36 months.
Primary Endpoint:	Mean change in the 24-hour rTNSS from baseline to 3 months after the study procedure.
Secondary Endpoints:	• Participant responder percentage, defined as the proportion of participants achieving a successful outcome at the 3-month evaluation. A successful outcome is defined as a 30% improvement (decrease) in the rTNSS. • Mean change in the Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ) score from baseline to 3 months after the study procedure. • Frequency of device-related and procedure-related serious adverse events through the 3-month evaluation.
Other Outcome Measures:	Adverse events - Incidence (type and category) of adverse events overall and by follow-up interval. Nasal Assessment – The target posterior nasal nerve area within each nostril will be visually assessed at baseline, following the treatment procedure and at 3 months. The use of an endoscope for visual assessment is required. Representative still photographs or video of each nostril will be captured for each assessment. Visual analog scale (VAS) for pain - perception of pain associated with the procedure on a 0 to 100 mm scale (0 indicating no pain and 100 indicating the worst pain ever) assessed posttreatment and at 3 months. rTNSS: • rTNSS mean and change from baseline at the 3-, 6-, 12-, 24- and 36-month follow-up evaluations. • rTNSS Individual Nasal Symptom Scores (rhinorrhea, nasal congestion, nasal itching, and sneezing) at baseline and at the 3-, 6-, 12-, 24-month and 36-month follow-up evaluations.

- Proportion of responders based on improvement in rTNSS at the 3-, 6-, 12-,24-and 36-month follow-up evaluations.

MiniRQLQ:

- MiniRQLQ mean and change from baseline at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
- MiniRQLQ domain scores (activity limitations, practical problems, nose symptoms, eye symptoms, and other symptoms) at baseline and the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.

Participant satisfaction assessment - Five-question self-reported survey of satisfaction with the procedure and recommendation to others administered at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.

Other rhinitis symptoms - current symptoms of cough and postnasal drip or excess mucous in the throat, rated on a 0 to 3 scale from 'No symptoms' to 'Severe symptoms', assessed at baseline and the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.

Change in amount of "as needed" medication/device use for chronic rhinitis symptoms - Self-reported assessment of an increase, no change, or decrease in medications and/or devices being used for treatment of symptoms compared to use prior to the procedure administered at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.

Medications - Medications associated with relief or treatment of nasal airway obstruction symptoms will be documented at baseline and updated as necessary at each evaluation. In addition, medications associated with treatment of adverse events will be documented.

Length of Study: The primary outcome will be evaluated at 3 months. In addition, evaluations at 6, 12, 24, and 36 months after treatment will extend follow-up to 3 years for evaluation of longer-term efficacy. Enrollment is anticipated to be completed within 6 months. Therefore, total study duration is anticipated to be approximately 42 months.

Study Centers: up to 20

Participants: Up to 140 subjects

Inclusion Criteria:

1. Age 18 to 85 years (inclusively).
2. Willing and able to provide informed consent.
3. Willing and able to comply with the subject-specific requirements outlined in the Study Protocol.

4. Seeking treatment for chronic rhinitis symptoms of at least 6 months duration and willing to undergo an office-based procedure.
5. Moderate to severe symptoms of rhinorrhea (rTNSS rating of 2 or 3 for rhinorrhea).
6. Mild to severe symptoms of nasal congestion (rTNSS rating of 1, 2 or 3 for congestion).
7. rTNSS ≥ 6.

Exclusion Criteria:

1. Anatomic obstructions that in the investigator's opinion limit access to the posterior nasal passage.
2. Altered anatomy of the posterior nose as a result of prior sinus or nasal surgery or injury.
3. Active nasal or sinus infection.
4. History of significant dry eye.
5. History of any of the following: chronic epistaxis, documented episodes of significant nose bleeds in the past 3 months, rhinitis medicamentosa, head or neck irradiation.
6. Have rhinitis symptoms only on a seasonal basis due to allergies.
7. Known or suspected allergies or contraindications to the anesthetic agents and/or antibiotic medications to be used during the study procedure session.
8. Known or suspected to be pregnant or is lactating.
9. Participating in another clinical research study.
10. Has any condition that predisposes to excessive bleeding.
11. Is taking anticoagulants (eg, warfarin, Plavix) or 325 mg aspirin that cannot be discontinued before the procedure.
12. Has previous procedure or surgery for chronic rhinitis.
13. Other medical conditions which in the opinion of the investigator would predispose the subject to poor wound healing, increased surgical risk, or poor compliance with the requirements of the study.

Schedule of Events

	Screening	Treatment		Follow-up				
				In office	Remote			
		Procedure	Immediate Postprocedure	3 Months[1] (13 weeks)	6 Months (26 weeks)	12 Months (52 weeks)	24 Months (104 weeks)	36 Months (156 weeks)
Window (days)	**(-30)**	**(0)**	**(0)**	**(± 14)**	**(± 30)**	**(± 30)**	**(± 30)**	**(± 30)**
Activity / Assessment								
Eligibility	X							
Consent	X							
Demographics / Medical History	X							
Physician Evaluations								
Nasal assessment (physical, endoscopic)	X	X	X	X				
Current medication use (study relevant)	X	X	X	X	X	X	X	X
Participant Evaluations								
VAS nasal pain			X	X				
Rhinitis symptoms (rTNSS, cough, and postnasal drip)	X			X	X	X	X	X
MiniRQLQ	X			X	X	X	X	X
Participant Satisfaction Survey				X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X

[1]Primary analysis endpoint.

List of Abbreviations

ADE – Adverse Device Effect

AE – Adverse Event

ANOVA – analysis of variance

AR – allergic rhinitis

BMI – Body Mass Index

CONSORT – Consolidated Standards of Reporting Trials

CRF (eCRF) – Case Report Form (electronic Case Report Form)

CTA – Clinical Trial Agreement

EC – Ethics Committee

EDC – Electronic data capture

ENT – Ear, Nose, Throat; medical field of otorhinolaryngology (otolaryngology)

EU – European Union

FDA – Food and Drug Administration (US)

FWA – Federalwide Assurance for the Protection of Human Subjects

GCP – Good Clinical Practice

ICH – International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

ICMJE – International Committee of Medical Journal Editors

IFU – Instructions for Use

IRB – Institutional Review Board

ISO – International Organization for Standardization

MCID – minimal clinically important difference

MDD – Medical Device Directive

MiniRQLQ – Mini Rhinoconjunctivitis Quality of Life Questionnaire

NAR – nonallergic rhinitis

PNN – posterior nasal nerve

PRN – Pro Re Nata (as needed or as required)

RF – Radiofrequency

RFTR – Radiofrequency turbinate reduction

rTNSS – Total Nasal Symptom Score (r, reflective)

SADE – Serious Adverse Device Effect

SAE – Serious Adverse Event

SD – standard deviation

UADE (USADE) – Unanticipated (Serious) Adverse Device Effect

VAS – Visual Analog Scale

1.0 Introduction and Background

Rhinitis is a condition in which the membrane lining the nasal cavity becomes irritated and swollen. Patients typically present with complaints of congestion, runny nose, sneezing, nasal itching, irritated throat, and postnasal discharge. The 2 major classifications of rhinitis are allergic rhinitis (AR) and nonallergic rhinitis (NAR). AR may be caused by allergens such as pollen, pet dander, mold, or dust. NAR may result from triggers that include chemicals, irritants, and medications.[1]

Chronic rhinitis may significantly impact a patient's quality of life by causing fatigue, headache, and sleep disturbance, resulting in cognitive impairment and diminished productivity, and thereby posing both a personal and financial burden.[2]

The nasal cavity is covered with an epithelial lining made of cells which interact to serve appropriate functions in the nasal environment.[3] Cells located in the epithelial lining include ciliated cells, goblet cells and seromucous glands. The goblet cell produces a carbohydrate called mucin which attracts water and forms a gelatin-like substance better known as mucus.[3,4] The goblet cell is the most prominent mucus producing cell in the nasal membrane and, together with the seromucous glands, works to provide mucus to the nasal mucosal surface. The purpose of mucus is to protect the body from substances that can enter through the nasal cavity. Secretion is stimulated by dust or foreign substances that enter the nasal passage. Mucus is cleared by movement of the cilia and disposed to the stomach.[4] Regulation of the seromucous glands and mucosal blood supply occurs through parasympathetic and adrenergic stimulation via the vidian nerve, posterior nasal nerves and other nerves. In some situations, the mucosa may become hyperresponsive to stimuli and produce excess mucus, resulting in rhinorrhea or postnasal discharge.

Patients presenting with runny or congested nose, watery eyes, irritated throat, and/or sneezing symptoms are evaluated to understand the types of triggers that may prompt the symptoms experienced. Understanding the patient's respiratory irritants may help differentiate between allergic or nonallergic responses.[2,5,6] Physicians can observe the nasal structures by transnasal endoscopy to rule out anatomic conditions mimicking rhinitis. Common anatomical obstructions that may cause rhinitis-like symptoms are nasal polyps, deviated septum, foreign bodies, nasal tumors and turbinate hypertropy.[1,2] Treatment of these anatomical causes, if present, may relieve rhinitis symptoms. The most common methods to determine allergy sensitivity are percutaneous skin testing and the allergen-specific immunoglobulin E (IgE) antibody testing. These tests can identify allergens the patient should avoid. However, if an allergic cause is eliminated through this testing, a diagnosis of nonallergic rhinitis could be made.[1,2]

Treatment to reduce symptoms may include nasal irrigation (nasal lavage) multiple times a day with a saline rinse, use of over-the-counter oral or nasal antihistamines and/or corticosteroid sprays, and allergen immunotherapy in AR patients. Patients with nonallergic rhinitis are less likely to respond to oral antihistamines, but may find their symptoms relieved with intranasal antihistamine, corticosteroid, or anticholinergic sprays. Patients whose symptoms are not adequately relieved with conservative treatment often seek treatment to alleviate symptoms and may be candidates for nasal

surgery. Vidian neurectomy is a surgical option to relieve chronic rhinitis symptoms as the vidian nerve supplies autonomic input to the nasal mucosa (as well as the palate and the lacrimal gland). While this surgery has been performed for over 50 years, it is controversial since access to the nerve can be technically difficult and complications with numerous surrounding important structures can occur.[7,8] Common procedural side effects include dry eyes, nasal dryness or crusting and mild pain. More significant risks may include hemorrhage, vision loss and palate/lip/cheek numbness. In addition, improvement in symptoms is often unpredictable.[7] An alternative neurectomy target is the posterior nasal nerve (PNN). The advantage of the PNN over the vidian nerve is its more limited innervation and activity on the nasal mucosa and its physical distance from other major nerve structures. As a result, complications associated with PNN surgery are less significant and occur less frequently than those described for vidian neurectomy,[7] while still providing significant improvement in quality of life.[9] A recent development is use of a cryosurgical probe to ablate PNN tissue.[10] Significant improvement from baseline in Total Nasal Symptom Score (TNSS) using this cryosurgical probe was observed.

Radiofrequency (RF) energy has been used for decades in the fields of otorhinolaryngology, neurosurgery, cardiology, urology and general surgery. ENT surgeons currently use radiofrequency energy in numerous nasal therapies, including radiofrequency turbinate reduction (RFTR), which is a minimally invasive surgical option that can reduce tissue volume in a precise, targeted manner. There have been multiple studies analyzing the safety and outcomes of using radiofrequency energy in the RFTR procedure.[11] The technique is well tolerated and effective. Numerous studies have also demonstrated that radiofrequency tissue therapy in the nasal passage can be safe and effective in improving nasal obstruction and in preserving nasal function.[12] Aerin Medical's radiofrequency system using the Vivaer® ARC Stylus has been investigated and shown effective in treatment of nasal airway obstruction.[13]

Aerin Medical previously conducted a small feasibility study (TP220) using the Aerin Medical radiofrequency system to treat subjects with chronic rhinitis. The InSeca® Stylus was used to apply radiofrequency energy to the inferior turbinate in the PNN area. At 6-months post procedure, 73% of subjects showed improvement in their Sino-Nasal Outcomes (SNOT-22) score. There were no device-related or procedure-related serious adverse events.

The feasibility study was followed by a prospective, nonrandomized multicenter study (TP668) with 50 participants that supported regulatory clearance of the RhinAer Stylus for treating rhinitis by targeting treatment to the portion of the inferior turbinate mucosa overlying the region of the PNN. The mean reflective Total Nasal Symptom Score (rTNSS) at baseline was 8.5 (SD 1.8) and improved to 3.4 (SD 2.3) at the 12-week primary endpoint (5.1-point or 59.2% improvement). The responder percent for at least a 1-point improvement in rTNSS at 12 weeks was 94%. Responder percent, based on at least 2-, 3- (~30%), and 4-point improvements in rTNSS were 92%, 88%, and 69%. Patient reported satisfaction with the procedure and quality of life improvement were high. No serious adverse events related to the device were observed and the limited number of adverse events possibly associated with the procedure or device were

relatively mild, transient, and not unexpected for this type of procedure. Together, the safety and efficacy results demonstrated the benefits of treating the PNN area of the nasal passageway with RF using the Aerin Medical procedure for relief of chronic rhinitis.

The current study is proposed to provide additional evidence for the effectiveness of the RF procedure.

2.0 Purpose

The purpose of this study is to assess the clinical use of the RhinAer Stylus to treat tissue in the posterior nasal nerve area to improve symptoms in adults diagnosed with chronic rhinitis.

2.1 Device and Regulatory Status

The RhinAer procedure will be performed in the study clinic using the RhinAer Stylus and Aerin Console. The RhinAer Stylus is a disposable handheld device capable of delivering bipolar radiofrequency energy to tissue when connected to the Aerin Console radiofrequency generating device.

The RhinAer Stylus was cleared for use in the United States (US) by the Food and Drug Administration (FDA) under 510(k) K192471 and the Aerin Console was cleared under 510(k) K162810. The RhinAer Stylus is has CE Marking in the European Union (EU). The Aerin Console has CE Marking in the EU.

2.2 Indications for Use (US)

The RhinAer Stylus is indicated for use in otorhinolaryngology (ENT) surgery for the destruction of soft tissue in the nasal airway, including in posterior nasal nerve regions in patients with chronic rhinitis.

The Aerin Console is an electrosurgical system intended to generate radiofrequency electrical current for the use of an Aerin Medical Stylus. The Aerin Console is indicated for use in small clinic, office or hospital environments.

2.3 Intended Use and Indications for Use (EU)

The RhinAer Stylus is intended to improve nasal breathing by modifying the soft tissues of the nasal airway. It is indicated for use in otorhinolaryngology (ENT) surgery for the destruction of soft tissue in the nasal airway, including in posterior nasal nerve regions in patients with chronic rhinitis. RhinAer Stylus has CE Marking in the EU.

The Aerin Console is an electrosurgical system intended to generate radiofrequency (RF) electrical current for modification of soft tissues during ear, nose and throat procedures, when used with an Aerin Medical Stylus. It is indicated for use in delivering radio-frequency energy to tissues as part of ear, nose and throat procedures in small clinic, office or hospital environments.

2.4 Rationale

Patients suffering from symptoms attributed to chronic rhinitis have treatment options ranging from medications to surgical procedures that have varying degrees of effectiveness, discomfort, and potential complications. There remains a significant need for a simple, safe, nonsurgical, minimally invasive treatment that can provide sustained relief for patients suffering with symptoms of chronic rhinitis. The RhinAer procedure using RF technology has been shown to be safe, effective and durable in a single-arm trial comparing pretreatment condition with posttreatment condition. This study is being undertaken to provide additional evidence of the effectiveness of the procedure.

3.0 Study Objectives

3.1 Primary Objective

The primary objective is to assess the performance of the RhinAer procedure with respect to improvement in the rTNSS from baseline to 3 months when used as a treatment for chronic rhinitis.

The primary objective will be assessed through evaluation of the primary endpoint defined as comparison of the mean rTNSS at baseline to the mean rTNSS at 3 months postprocedure.

3.2 Secondary Objectives

Additional objectives include assessment and comparison of secondary endpoints and informational outcome measures.

Secondary endpoints are:

- Participant responder percentage at 3 months. Individual participant success (responder) is defined as at least 30% improvement (decrease) in the 24-hour reflective Total Nasal Symptom Score (rTNSS).
- Mean change in the Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ) score from baseline to 3 months after the study procedure.
- Frequency of device-related and procedure-related serious adverse events through the 3-month evaluation.

Informational outcomes include:

- Adverse events - Incidence (type and category) of adverse events overall and by follow-up interval.
- Nasal Assessment - The target PNN area within each nostril will be visually assessed at baseline and following the treatment procedure at all evaluations. The use of an endoscope for visual assessment is required. Representative still photographs or video of each nostril will be captured at each visit.

- Visual analog scale (VAS) for pain - perception of pain associated with the procedure on a 0 to 100 mm scale with 0 indicating no pain and 100 indicating the worst pain ever posttreatment through 3 months.
- rTNSS:
  - rTNSS mean and change from baseline at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
  - rTNSS Individual Nasal Symptom Scores (rhinorrhea, nasal congestion, nasal itching, and sneezing) at baseline and the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
  - Proportion of responders based on improvement in rTNSS at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
- MiniRQLQ:
  - MiniRQLQ mean and change from baseline at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluation.
  - MiniRQLQ domain scores (activity limitations, practical problems, nose symptoms, eye symptoms, and other symptoms) at baseline and the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
- Participant satisfaction assessment - Five-question self-reported survey of satisfaction with the procedure and recommendation to others summarized by question at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
- Other rhinitis symptoms - current symptoms of cough and postnasal drip or excess mucous in the throat, rated on a 0 to 3 scale from 'No symptoms' to 'Severe symptoms', assessed at baseline and the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
- Change in amount of PRN medication/device use for chronic rhinitis symptoms - Self-reported assessment of an increase, no change, or decrease in medications being used for treatment of symptoms compared to use prior to the procedure summarized by category at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
- Medications - Medications associated with relief or treatment of chronic rhinitis symptoms will be documented at baseline and updated as necessary at each evaluation. In addition, medications associated with treatment of adverse events will be documented.

3.3 Safety and Risk Profile

The safety and risk profile of the RhinAer procedure will be evaluated with respect to overall incidence of adverse events and treatment-related adverse events.

4.0 Study Plan

4.1 Study Design

The study is designed as a multicenter (up to 20 sites), prospective, open-label, single-arm study in up to 140 participants.

All participants will be evaluated prior to treatment and following treatment at week 13 (3 months). The 3-month evaluation will occur in the physician's office and be used for the primary analysis.

The study will have additional follow-up evaluations at 6, 12, 24, and 36 months conducted by phone interview to provide additional information on longer-term safety and duration of treatment effect.

4.2 Study Population

The target population for this study is adults who have exhibited symptoms of chronic rhinitis, such as congestion, rhinorrhea, sneezing, and itching, that may be caused by nonallergic or allergic triggers for at least 6 months. Patients with symptoms due only to seasonal allergies are to be excluded. This study requires significant symptoms demonstrated by an rTNSS ≥ 6, which includes moderate to severe symptoms of rhinorrhea and mild to severe symptoms of nasal congestion.

Patients who have anatomic obstructions that may limit access to the target treatment area or have altered posterior nasal anatomy due to prior surgery or injury are excluded from participation.

Patients must meet all inclusion and exclusion criteria listed below for participation in the study.

4.2.1 Inclusion Criteria

1. Age 18 to 85 years (inclusively).
2. Willing and able to provide informed consent.
3. Willing and able to comply with the participant-specific requirements outlined in the Study Protocol.
4. Seeking treatment for chronic rhinitis symptoms of at least 6 months duration and willing to undergo an office-based procedure.
5. Moderate to severe symptoms of rhinorrhea (rTNSS rating of 2 or 3 for rhinorrhea).
6. Mild to severe symptoms of nasal congestion (rTNSS rating of 1, 2 or 3 for congestion).
7. rTNSS ≥ 6.

4.2.2 Exclusion Criteria

1. Anatomic obstructions that in the investigator's opinion limit access to the posterior nasal passage.

2. Altered anatomy of the posterior nose as a result of prior sinus or nasal surgery or injury.
3. Active nasal or sinus infection.
4. History of significant dry eye.
5. History of any of the following: chronic epistaxis, documented episodes of significant nose bleeds in the past 3 months, rhinitis medicamentosa, head or neck irradiation.
6. Have rhinitis symptoms only on a seasonal basis due to allergies.
7. Known or suspected allergies or contraindications to the anesthetic agents and/or antibiotic medications to be used during the study procedure session.
8. Known or suspected to be pregnant or is lactating.
9. Participating in another clinical research study.
10. Has any condition that predisposes to excessive bleeding.
11. Is taking anticoagulants (eg, warfarin, Plavix) or 325 mg aspirin that cannot be discontinued before the procedure.
12. Has previous procedure or surgery for chronic rhinitis.
13. Other medical conditions which in the opinion of the investigator would predispose the subject to poor wound healing, increased surgical risk, or poor compliance with the requirements of the study.

4.3 Enrollment

Patients diagnosed with chronic rhinitis and meeting all eligibility criteria may be enrolled in the study.

4.4 Outcome Measures

4.4.1 Nasal Assessment

The target PNN area within each nostril will be visually assessed at baseline (pretreatment), immediately following the treatment procedure, and at 3-month evaluation. The use of an endoscope for visual assessment is required. Observations are categorized as not present, mild, moderate, or severe. Representative still photographs or video of each nostril will be captured at each visit.

Assessments include:

- Significant dry eye (yes/no)
- Bruising around orbital area
- Soreness, pain
- Numbness

Endoscope required:

- Inflammation / generalized redness
- Swelling, edema
- Bleeding at anesthetic injection site (not requiring physician intervention)
- Bleeding at treatment site (not requiring physician intervention)
- Nasal obstruction from tissue edema
- Disruption of mucosal flow / crusting.

4.4.2 Pain – Visual Analog Scale Pain Score

A horizontal 100 mm VAS[14] anchored on the left with the words "No Pain" and on the right with the words "Worst Pain Imaginable", will be used to measure nasal pain associated with the procedure. Scores are obtained by measuring the distance in millimeters from the left origin of the line (0) to the point indicated with a slash placed by the participant to indicate their current level of pain in and around the nose.

4.4.3 Total Nasal Symptom Score (TNSS)

The TNSS is an instrument used to collect patient self-rated severity of nasal symptoms originally comprised of 3 symptoms (nasal obstruction, itching/sneezing and secretion/runny nose)[15] that has been widely adapted to include 4 nasal symptoms: rhinorrhea, nasal congestion, nasal itching, and sneezing. The FDA has cited the TNSS as a preferred measure of efficacy in trials of drug treatments for allergic rhinitis[16] and nonallergic rhinitis.[17] The TNSS requires the patient to rate 4 nasal symptoms (rhinorrhea, nasal congestion, nasal itching and sneezing) on the following 4-point scale:

- 0 = absent symptoms (no sign/symptom is evident)
- 1 = mild symptoms (sign/symptom present, but minimal awareness; easily tolerated)
- 2 = moderate symptoms (definite awareness of sign/symptom that is bothersome but tolerable)
- 3 = severe symptoms (sign/symptom that is hard to tolerate; causes interference with activities of daily living and/or sleeping).

The total score is the sum of the 4 nasal symptom scores with a maximum TNSS of 12 indicating the most severe symptoms.

The minimal clinically important difference (MCID) for change in mean TNSS derived from anchor-based methodologies has been shown to be 0.23 - 0.28 units and by distribution-based methodology the MCID was determined to be 0.59 units.[18] A less rigorous expert panel-based estimate of the MCID was 30% of the maximum score of 12, which is 3.6 units.[19] The evidence-based

thresholds for MCID have been recommended to supersede the panel-based method.[20,21]

The 24-hour reflective TNSS (rTNSS) will be used in this study. Participants will be asked to self-evaluate their symptom severity over the preceding 24 hours.

Treatment Responder based on rTNSS improvement

Individual participant success (responder) is defined as at least 30% improvement (decrease) in the rTNSS from baseline.

4.4.4 Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ)

The Rhinoconjuctivitis Quality of Life Questionnaire is a well-established, validated, and the most frequently used rhinoconjuctivitis disease-specific instrument.[22] The original RQLQ consisted of 28 questions across 7 domains and included ratings of 3 activities selected by the patient.[23] The validated standardized version (RQLQ(S)) uses standardized activity questions, which facilitates ease of administration.[24] The MiniRQLQ, to be used in this study, was developed and validated to further facilitate ease of use and efficiency by reducing the number of questions to 14.[25] The RQLQ(S) and the MiniRQLQ were found to be the best tests with optimal discriminant validity and responsiveness for measurement of health-related quality of life in AR patients.[26] While much of the development and validation of the RQLQ instruments have occurred in AR patients, the MiniRQLQ has also been validated for NAR patients.[27]

The instrument consists of 14 questions across 5 domains (activity limitations (n=3), practical problems (n=2), nose symptoms (n=3), eye symptoms (n=3), and other symptoms (n=3)). Responses are based on a 1-week recall and provided on a 7-point scale:

- 0 = not troubled
- 1 = hardly troubled at all
- 2 = somewhat troubled
- 3 = moderately troubled
- 4 = quite a bit troubled
- 5 = very troubled
- 6 = extremely troubled.

The total or overall MiniRQLQ score is the mean of the 14 responses and the domain scores are the mean of the questions in each domain.

The generally accepted MCID for the overall RQLQ(S) and each individual domain is 0.5[22,24,28,29] and has also been reported as ≥ 0.62.[30] The developers of the RQLQ instruments reported that the MCID for the MiniRQLQ was slightly

higher (0.7) than for the RQLQ(S).[25] Another study using a combination of both anchor-based and distribution-based methods determined the MCID for the MiniRQLQ to be 0.42 (95% confidence interval 0.30 - 0.51).[31]

4.4.5 Participant Satisfaction

Satisfaction with the procedure is measured with a five-question self-reported survey using a 5-point scale to assess tolerability of the procedure, ease of recovery, change in drainage/rhinorrhea/runny nose symptoms, overall satisfaction with the procedure, and recommendation to others

4.4.6 Other Rhinitis Symptoms - Cough and Postnasal Drip

Self-reported assessment of current problems with cough and postnasal drip or excess mucous in the throat rated on the same 4-point scale used for symptoms comprising the rTNSS:

- 0 = absent symptoms (no sign/symptom is evident)
- 1 = mild symptoms (sign/symptom present, but minimal awareness; easily tolerated)
- 2 = moderate symptoms (definite awareness of sign/symptom that is bothersome but tolerable)
- 3 = severe symptoms (sign/symptom that is hard to tolerate; causes interference with activities of daily living and/or sleeping).

4.4.7 Change in Amount of PRN Medication/Device Use for Chronic Rhinitis Symptoms

Self-reported assessment of an increase or decrease from baseline in as needed medications and/or devices used for treatment of nasal symptoms following the procedure.

4.4.8 Medication and Other Therapies for Symptoms of Chronic Rhinitis

The current use of medication, devices, or other therapies for symptoms of chronic rhinitis, medication name, frequency, and dose will be recorded at each evaluation visit. Medications may be categorized for reporting purposes.

4.4.9 Adverse Events

Adverse events will be documented according to Section 7.1.

4.5 Success/Failure Criteria

Determinations of the successfulness of the treatment will be made on 2 levels: the individual participant level and in terms of the overall change in mean rTNSS from baseline to 3 months after the procedure.

4.51 Participant Success

The success measure for individual participant success (responder) is defined as at least 30% improvement (decrease) in the rTNSS from baseline at the 3-month primary endpoint.

4.5.2 Participant Failure

A participant will be considered a nonresponder at the 3-month evaluation if the success criterion has not been attained.

4.5.3 Study Success

The study will be considered a success if the mean change from baseline of the rTNSS at 3 months significantly exceeds the MCID set for the study.

4.6 Duration of the Study

The primary outcome will be evaluated at 3 months. In addition, evaluations at 6, 12, 24, and 36 months after treatment will extend follow-up to 3 years for evaluation of longer-term efficacy. Enrollment is anticipated to be completed within 6 months. Therefore, total study duration is anticipated to be approximately 42 months.

4.7 Site Staffing and Responsibilities of Study Personnel

The principal investigator is responsible for ensuring that he/she has sufficient and qualified staff to conduct the clinical study and that all study-related tasks have been appropriately delegated and documented.

The treating physician will perform the procedure and discharge and 3-month follow-up assessments. The treating physician must be a medical doctor with experience in ENT procedures and trained in administering the RhinAer procedure.

Remote follow-up will be performed by medical or office staff with relevant knowledge and experience as determined by the principal investigator to interact with study participants to ensure collection of study data and participant reported outcomes.

4.8 Device Description

The RhinAer procedure incorporates use of the RhinAer Stylus (Model FG815), which is a cleared (FDA - K192471) disposable handheld device capable of delivering bipolar radiofrequency energy to tissue. RhinAer has CE Marking in EU. The Aerin Console (Model FG226) RF generator with temperature control capable of delivering very low doses of energy was cleared for use in the US (FDA - K162810) and has CE Marking in the EU (CE639608)

The RhinAer Stylus (Figure 1) consists of a handle, shaft and treatment tip. An array of bipolar electrodes is positioned on a nonconductive tip (Figure 2) that is attached to the handle via a nonconductive shaft. A temperature sensor is located on the Stylus tip to monitor tissue temperature during RF energy delivery. The Stylus is powered by an external temperature-controlled radiofrequency generator via a flexible cable (Figure 3). The Stylus incorporates features to allow compatibility with and

authentication by only the Aerin Console. The connector for the RhinAer Stylus has a pin configuration that prevents its use with other RF generators, making it only compatible with the Aerin Console. Authentication of the Stylus is achieved via a crypto chip that is built into the Stylus handle assembly. The chip is read and written to by the Aerin Console. Information stored on the chip includes the Stylus model information, default treatment parameters (Power 4W, Temperature 60 °C, Duration 12s, Cooling Time 0s), custom treatment setting ranges (Power 3-5W, Temperature 50-70°C, Duration 10-18s, Cooling 9-12s), usage timestamp data, and a count of the remaining treatment cycles (based upon pre-set maximum).

The RhinAer Stylus is temporarily inserted into the nose to access the treated area. The Stylus requires the application of conductive media to the treatment tip prior to use. The conductive media helps to ensure good contact with tissue at all points of the treatment tip to facilitate energy transmission. Application of the RF energy is controlled by a foot switch connected to the Console. The RhinAer Stylus treats symptoms of chronic rhinitis by modifying the tissues of the nasal airway through the use of low doses of radiofrequency energy to destroy tissue in the PNN regions. The low-power radiofrequency energy generates heat within the submucosal tissue, destroying local tissue, mucous cells, and glands, and creating a coagulation lesion. This destruction of tissue in PNN regions improves symptoms of chronic rhinitis.

The procedure requires local anesthesia only. The Stylus is manufactured and supplied sterile and for single use only by Aerin Medical and may be used to treat both nostrils of the patient.

Figure 1. RhinAer Stylus

Figure 2. RhinAer Stylus tip

Figure 3. Aerin Console with RhinAer Stylus

4.9 Risk/Benefit Analysis

4.9.1 Risks

Potential risks associated with the use of the RhinAer Stylus do not differ from commonly used devices and treatments for chronic rhinitis, but due to the nonsurgical nature of the therapy, small treatment area, low energy delivery,

and lack of need for general anesthesia, the overall risk to the participant may be less than presented by other surgical treatments.

Potential risks associated with the use of the RhinAer Stylus and the associated local anesthetics are listed below. Participants will be monitored closely as part of this study to allow for early detection of potential problems and prompt treatment if required.

Adverse events or side effects that may occur as a result of the treatment include:

- External deformity
- Blanching (generalized whiteness)
- Bruising including around the orbital area (black eyes)
- Infection
- Bleeding (other than during the treatment at treatment sites and greater than anticipated by the investigator)
- Mucosal changes
- Scar formation leading to nasal obstruction
- Sensory changes at treatment site
- Dry eye
- Vasovagal response secondary to the procedure

Anticipated observations that are expected in and around the treatment area and are considered minor include:

- Inflammation / generalized redness
- Temporary swelling, edema
- Temporary numbness/tingling
- Temporary soreness/pain
- Mild bleeding at anesthetic injection and/or treatment site (not requiring physician-level intervention, such as cautery)
- Temporary nasal obstruction from tissue edema
- Disruption of mucosal flow/intranasal crusting
- Scab formation.

These observations will be assessed in the nasal assessment and recorded at study visits if they occur. Should any of the following require mitigation by the treating physician or be greater in severity or degree of incidence than

anticipated, they will be considered an adverse event and will be recorded on the study Adverse Event CRF.

Symptomatic improvements may not be achieved in all participants receiving the RhinAer procedure and may not be durable beyond the 3-month evaluation in all participants with relief at 3 months.

4.9.2 Mitigation of Risks

The study was developed based on previous preclinical and clinical experience and includes a number of steps to minimize any additional risks to participants in the study:

- Careful consideration has been given to the inclusion/exclusion criteria in order to select appropriate candidates for treatment.
- Patients will be fully informed of the study requirements prior to enrollment.
- Only physicians with experience in nasal surgical and minimally invasive procedures, and with specific training using the RhinAer Stylus for performing the RhinAer procedure will be permitted to participate in the study.
- The study will be reviewed and approved by an IRB(s)/EC(s) and conducted according to applicable regulations with ongoing review by the IRB/EC.
- Study procedures, follow-up, and study monitoring are designed to detect and respond to any adverse events in a timely manner.
- Preclinical mechanical and bench evaluations have been conducted to demonstrate that the design characteristics of the study device are appropriate for reliable clinical use of the device.
- The Console has been cleared for use in the US by the FDA based in part on prior clinical studies demonstrating safety and efficacy of its use and CE Marking in the EU. The RhinAer Stylus is also cleared for use by the FDA based in part on prior clinical studies demonstrating safety and efficacy of use, and has CE Marking in the EU.

4.9.3 Benefits

The potential benefit associated with the RhinAer procedure is to offer a minimally invasive treatment method that has been shown in a previous study to help alleviate symptoms of chronic rhinitis and which has been cleared for use by the FDA. The RhinAer procedure treats symptoms of chronic rhinitis by modifying the tissues of the nasal airway through the use of low doses of radiofrequency energy to destroy tissue in the PNN regions. The low-power radiofrequency energy generates heat within the submucosal tissue, destroying local tissue, mucous cells, and glands, and creating a coagulation lesion. This

destruction of tissue in PNN regions improves symptoms of chronic rhinitis. These benefits may last beyond the length of the study.

The procedure will be provided at no cost to participants.

4.9.4 Potential Risks to Participant Confidentiality

In all clinical studies, confidentiality of protected health information may be breached due to study-related activities beyond those of routine clinical care. This risk will be minimized by not entering personally identifying information into the electronic data capture (EDC) system through the study's electronic case report forms (eCRF). Risks to participant confidentiality are further minimized by allowing only authorized individuals to access the EDC system and the database that stores the electronically entered data. The 21CRF Part 11 compliant and validated system maintains audit trails on all entries, changes or corrections to eCRFs. If a person with authority to complete but not sign eCRFs makes changes to an already signed eCRF, the investigator will be required to re-sign the eCRF, thereby protecting the integrity of the data collection process and the data.

4.9.5 Study Justification in Relation to Risk

The study sponsor believes that any additional risks presented by participating in this study are very low and that adequate testing, safeguards, and risk monitoring have been incorporated into the study to further minimize and mitigate the risks relative to the potential benefits, including relief from symptoms of chronic rhinitis, that may be realized by participation in this study.

5.0 Study Schedule and Procedures

This section provides summaries of the study schedule of events and flow of participants through the study, as well as more detailed information on study procedures and processes.

5.1 Schedule of Events

	Screening	Treatment		Follow-up				
				In office	Remote			
		Procedure	Immediate Postprocedure	3 Months[1] (13 weeks)	6 Months (26 weeks)	12 Months (52 weeks)	24 Months (104 weeks)	36 Months (156 weeks)
Window (days)	**(-30)**	**(0)**	**(0)**	**(± 14)**	**(± 30)**	**(± 30)**	**(± 30)**	**(± 30)**
Activity / Assessment								
Eligibility	X							
Consent	X							
Demographics / Medical History	X							
Physician Evaluations								
Nasal assessment (physical, endoscopic)	X	X	X	X				
Current medication use (study relevant)	X	X	X	X	X	X	X	X
Participant Evaluations								
VAS nasal pain			X	X				
Rhinitis symptoms (rTNSS, cough, and postnasal drip)	X			X	X	X	X	X
MiniRQLQ	X			X	X	X	X	X
Participant Satisfaction Survey				X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X

[1]Primary analysis endpoint.

5.3 Enrollment and Baseline Assessment

Screening

The investigator or designated research staff will perform an evaluation of the study candidate for study eligibility, which may include a history and physical examination of the nasal area, review of overall medical history, understanding of general health and discussion of any conservative measures used chronic rhinitis. In addition, patients will complete standard questionnaires to document current symptoms associated with chronic rhinitis (rTNSS, MiniRQLQ).

Patients must be diagnosed with chronic rhinitis prior to entry into the study. The use of diagnostic procedures and screening tests to determine a diagnosis and assess whether patients are appropriate candidates for inclusion in the study is an appropriate pre-entry activity. While the availability of the study may be discussed with a prospective participant without first obtaining consent, informed consent must be obtained prior to initiation of any clinical procedures dictated by the protocol that are performed solely for the purpose of determining eligibility to participate in the study. Once the pretreatment assessments are completed the study procedure should be scheduled within 30 days.

Informed consent

Informed consent must be obtained in accordance with FDA regulation 21 CFR Part 50 and ISO 14155. The clinical investigator or designated staff member is responsible for ensuring that IRB/EC approved informed consent is obtained for each participant prior to participation in the study or before undergoing any procedure specific to the clinical investigation. The patient must be fully counseled with an explanation of the study background, study procedure, follow-up schedule, and informed of their options, risks and benefits, and have every opportunity to ask questions about participation in the study. Any new information obtained during the course of the study that may affect the health of the participant or their decision to continue in the study will be provided to the participant. This process includes a thorough explanation of the informed consent document that the patient will be asked to sign acknowledging that they understand and desire to participate in the study. The explanation and discussion should be conducted in such a way as to:

- answer the participant's questions,
- avoid coercion or influence of patient to participate in the study,
- ensure the patient understands that their legal rights are not waived at any time,
- use language at a level the patient can understand, and
- ensure the patient understands that after providing signature on the Informed Consent, the patient may still withdraw at any time before, during or after study treatment.

Evaluation of inclusion and exclusion criteria

The Screening Visit / Study Eligibility CRF will be used to document the participant's eligibility status.

Pretreatment (baseline) data and assessments

The following data will be obtained prior to treatment and recorded on the Baseline Visit Demographics and Treatment History CRF:

- Demographics
  - Sex
  - Height (inches)
  - Weight (pounds)
  - Date of birth
  - Race / Ethnicity
- Nasal symptoms, history of treatments, nasal visual exam
  - History (duration) of rhinitis

- Rhinitis triggers (allergic or nonallergic)
- Medications used to treat rhinitis
- Previous ENT treatments
- Turbinate enlargement, nasal polyps, and other significant findings

The nasal assessment data (each nostril) including photos or video (physical and endoscopic) will be recorded and entered into the eCRF.

Current use of medication, devices, or other therapies for symptoms of chronic rhinitis, including medication name, frequency, and dose will be detailed on the Medication Log.

Rhinitis symptom severity, including the rTNSS, cough and postnasal drip, will be completed by the participant on the rTNSS CRF.

The MiniRQLQ will be completed by the participant on the MiniRQLQ CRF.

5.4 Treatment Visit and Procedure

If the participant meets eligibility criteria and signs the IRB/EC approved informed consent the participant is considered enrolled.

The treatment procedure is summarized below. Consult the RhinAer Stylus and Aerin Console Instructions for Use (IFUs) for full detail of the treatment procedure and step-by-step instructions for preparation and use of the RhinAer Stylus and Aerin Console.

Preparation

The procedure will be performed in the study clinic. The participant will be in a reclined or supine position on the procedure table. A visual physical and endoscopic nasal assessment will be conducted just prior to the procedure and documented on the appropriate CRF. The study physician will map out the treatment area by evaluating the middle meatus and surrounding structures of the nasal cavity to understand access of the study device to the mucosal area for treatment. Participants will have both PNN areas treated in a single study procedure session. Each nostril will be treated at up to 5 nonoverlapping positions within the posterior portion of the middle meatus and posterior portion of the inferior turbinate (Figure 4).

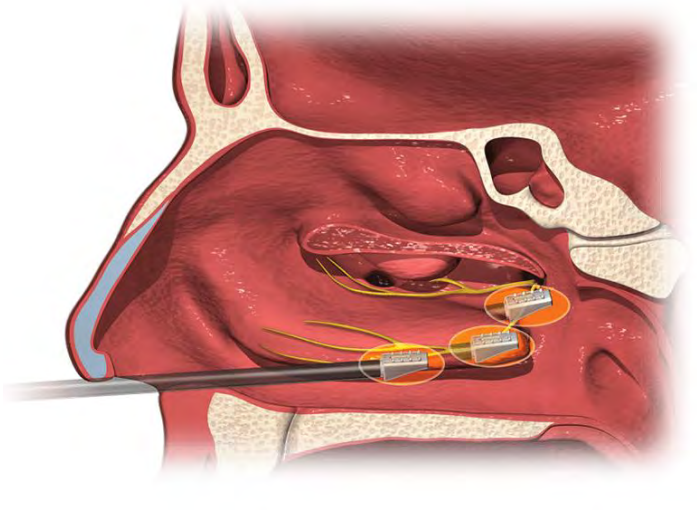

Figure 4. RhinAer Stylus in the nose.

The physician will anesthetize the treatment area by using a topical swab/gauze or spray of lidocaine to numb the mucosal tissue, wait a minimum of 20 minutes, and then inject anesthesia to the treatment area after initial numbness has occurred.

Treatment administration

An endoscope will be inserted into the nasal cavity so the physician can visualize the mucosal area of treatment. The RhinAer Stylus will then be inserted to access the treatment area. The Stylus will be connected to the Aerin Console generator and the RF energy level will be set on the generator.

The default settings for the RhinAer Stylus will be used for the study:

Temperature	60 °C
Power	4 Watts
Treatment Time	12 secs
Cooling Time	0 secs

The physician will apply the treatment tip of the RhinAer Stylus to the target tissue prior to energy delivery. The energy is turned on by maintaining downward pressure on the foot pedal. With the energy on, the physician continues to apply the Stylus tip to the mucosal surface consistent with the IFU. A tone will be heard when energy is being delivered until the treatment is complete. After the treatment time is reached, the Aerin Console will cease to delivery energy and reset for subsequent treatments.

No repeat ("touch-up") procedures will be permitted during the study follow-up period.

Procedure data collection

Data relating to the procedure and the products used will be recorded on the Procedure CRF. The following information will be recorded:

- Date of procedure

- Preprocedure nasal assessment (each nostril) including photos or video (physical and endoscopic)
- Preprocedure and procedure medications
- RhinAer Stylus and Aerin Console information
- Aerin Console settings
- Procedure start and end times
- Number of sites treated
- Occurrence of device malfunction, protocol deviation, or adverse events.

5.5 Postprocedure Assessments and Care

An endoscopic nasal assessment will be conducted prior to discharging the participant and reported on the Procedure CRF.

Participants will be asked to indicate the pain level experienced during the study procedure from anesthesia delivery to procedure completion using the VAS pain score instrument (vertical line marked on the 100 mm line) on the Pain VAS CRF.

At the discretion of the physician, the following care may be provided:

- Apply compression to the treatment area internally for 5 minutes.
- Apply petroleum jelly to the treatment area as needed.
- Use of nasal saline spray or ointment as needed.
- The participant should be instructed not to blow their nose for 24 hours.

Participants should have their 3-month follow-up visit (13 weeks) scheduled within the visit window prior to release.

Participants should not generally receive other concomitant nasal treatment therapies or interventions after the procedure or during the study follow-up period to avoid confounding the evaluation of the effect of the treatment, unless the additional care is in response to an adverse event or is considered in the best interest of the participant. Therapies, interventions, and pain medication will be monitored at follow-up evaluations.

5.6 Follow-up Evaluations

Follow-up visit dates will be calculated from the study procedure date. Follow-up visits should be scheduled within the specified visit windows described in Section 5.1 and Table 1 (Section 8.3.2). The office follow-up evaluation occurs at 13 weeks after the procedure. Evaluations at 6, 12, 24, and 36 months will be conducted remotely by telephone assessment by site personnel. The timing of all follow-up evaluations is based on the date of the procedure and should not be altered based on the actual time of preceding follow-up visits. Participants who make nonstudy visits should be evaluated for possible adverse events and an Adverse Event CRF should be submitted if appropriate.

All participants should be followed through the final evaluation visit at 3 years postprocedure regardless of their success/failure classification at previous evaluations. Every effort should be made to avoid having participants withdraw from the study (Section 9.5). If a participant does choose to withdraw from the study, it is very important to record information regarding the reason(s) and the last known status of the participant.

The following assessments will be conducted as indicated for each follow-up time point and recorded on the corresponding CRFs:

Office evaluation at 13-week (3-month) follow-up

- Nasal assessment (each nostril) including photos or video
- Current use of medication, devices or other therapies for symptoms of chronic rhinitis, including medication name, frequency, and dose
- Participant reported change in use of as needed medications and devices for chronic rhinitis symptoms (completed by participant)
- rTNSS (completed by participant)
- Cough and postnasal drip symptoms (completed by participant)
- MiniRQLQ (completed by participant)
- VAS pain score (completed by participant)
- Adverse events.

Remote (telephone) evaluations: 6-month (26-week), 12-month (52-week), 24-month (104-week), and 36-month (156-week) follow-up

- rTNSS (verbal administration by site personnel)
- Cough and postnasal drip symptoms (verbal administration by site personnel) (no 2-week)
- MiniRQLQ (verbal administration by site personnel)
- Participant reported change in use of as needed medications and devices for chronic rhinitis symptoms (verbal administration by site personnel)
- Patient satisfaction survey (verbal administration by site personnel)
- Current use of medication or other therapies for symptoms of chronic rhinitis, including medication name, frequency, and dose (study staff follow-up required if participant indicates changes)
- Adverse events (study staff follow-up required if participant indicates changes).

5.7 Product Handling and Accountability

A system that allows tracking of orders, shipping and returns will be used to control RhinAer Stylus and Aerin Console inventory. The devices will be packaged and

labeled to clearly indicate that they are for clinical study use only and must only be used for participants enrolled in this study. All devices not used must be returned to the sponsor or disposed of in accordance with the sponsor's instructions. The investigator is responsible for adequate record keeping regarding the receipt, use, and final disposition of study inventory.

6.0 Statistical Considerations

6.1 Study Design

This is a prospective, multicenter, open-label, single-arm study to assess the performance of the RhinAer procedure for treatment of chronic rhinitis. The study is designed to assess improvement in rTNSS and other measures from baseline condition to 3 months after the procedure, as well as for extended follow-up through 3 years.

6.2 Study Hypothesis

The primary endpoint of the study is change in mean rTNSS from baseline to the 13-week evaluation. Improvement in the rTNSS is represented by a decrease from baseline in the 12-point score.

An MCID of 1 unit, or 2 to 4 times the more rigorously derived MCIDs, was set for this study. The hypothesis is that the improvement (decrease) in rTNSS mean score, measured as change from baseline at 13 weeks (13 weeks - baseline), exceeds the MCID (1 unit).

The null (H_0) and alternative (H_A) hypotheses are:

H_0: $\mu_d \geq -1$

H_A: $\mu_d < -1$

where μ_d = the mean change of the paired differences of the 13-week scores minus the baseline scores.

Rejection of the null hypothesis in favor of the alternative (H_A) hypothesis means that there is evidence for a clinically significant improvement (decrease) in the rTNSS.

6.3 Sample Size Estimate

The study will enroll up to 140 participants. The power analysis was performed such that there is adequate power to reject the null hypothesis that the mean improvement from baseline in rTNSS is 1 point or less. Sample size estimation was based on a paired t-test for change from baseline at 13 weeks using the following assumptions:

- Significance level $\alpha = 0.025$ (one-sided)
- Power = 90%
- μ_d = 1-point decrease in mean change score = MCID
- SD = 3 = estimated standard deviation of the mean difference based on an observed SD of 2.6 in a prior study.

The minimum number of subjects to achieve 90% power is 97 (G-Power, paired t-test). Allowing for 15% loss (nonevaluable) and adjusting for a balanced distribution across 20 sites the sample size is 140 participants. It is anticipated that participants will be enrolled at sites on a competitive basis; however, a reasonable balance of participants among sites may be maintained by potentially capping enrollment at individual sites based on the final number of participating sites.

6.4 Timing of Analysis

The primary evaluation phase of the study lasts until all participants have reached the primary endpoint at 13 weeks (3 months) postprocedure. The primary and secondary endpoints will be analyzed using the data from the primary evaluation phase for an interim study report when these data become available. Informational outcomes will be analyzed and included in interim reports after all participants have reached each of the successive follow-up time points. A final study report will be provided after all participants have reached the final follow-up evaluation of the extended follow-up phase of the study.

6.5 Analysis Populations

Enrolled Population – all subjects enrolled in the study.

Evaluable Population – all subjects that are enrolled in the study and have received the study procedure.

Safety Population – all subjects enrolled in the study.

6.6 Missing Data

All efforts will be made to collect all data points in this study. Missing data will be imputed for the primary endpoint by assuming the missing outcomes represent no change from baseline. Additional post hoc sensitivity analyses may be performed if missing cases exceed 10% of the sample size, including a worst-case analysis (all missing rTNSS at 3 months are the worst possible score), to further assess the effect of missing data on the primary analysis. The results of the sensitivity analysis will not be used to adjust the conclusions drawn from the primary analysis.

Secondary outcome measures and additional observational measurements will be analyzed by using available data only.

6.7 Pooling

All study data will be pooled across study sites to facilitate hypothesis testing in accordance with the sample size estimation and power analysis (Section 6.3). Pooling is generally justified because the study will be conducted such that: 1) the same protocol will be used at each site; 2) site investigators and personnel will receive uniform training; and 3) central data management and monitoring will be consistent and applied with equal rigor at all sites. Comparability between study sites may be shown using summary statistics calculated by site.

6.8 Participant Disposition

A detailed description of participant disposition will be provided using a CONSORT diagram and summaries of participants falling in various subgroups of interest, such as, enrolled but not treated, discontinued, protocol deviations, deaths, and withdrawals. All study population exclusions and reasons will be summarized. Follow-up by visit will be presented, showing theoretical, expected, and actual follow-up visits.

6.9 Demographics and Baseline Characteristics

Demography and other baseline characteristics will be summarized using frequencies and percentages for categorical factors and mean, median, standard deviation, minimum and maximum for continuous factors. Demographic characteristics will be reported to describe the profile of samples.

Baseline covariates with possible impact on outcomes at 3 months are:

- Age
- Race
- Sex
- BMI
- Allergic status (allergic rhinitis - nonallergic rhinitis).

Results may be evaluated by allergic status if sufficient numbers are obtained in both categories.

6.10 Primary Endpoint Analysis

The mean change in the rTNSS from baseline to 13 weeks will be tested using a paired t-test for a significant decrease greater than the MCID under the one-sided null and alternative hypotheses.

A *P* value for the test statistic $\leq$.025 will indicate that the mean decrease is statistically significantly greater than 1 point. The upper limit of the one-sided 97.5% confidence interval on the mean decrease will also be calculated.

6.11 Secondary Endpoints Analysis

Secondary endpoints will be formally tested only after the primary objective of the study is met. Confidence intervals (95%) will be included for all secondary outcome measures.

- Responder percentage at 13 weeks

  The proportion of responders will be calculated along with the 95% confidence interval. Individual participant success (responder) is defined as at least 30% improvement (decrease) in the 24-hour reflective Total Nasal Symptom Score (rTNSS). An overall responder percent of at least 60% is

expected for the study. The observed proportion of responders will be compared to the expected proportion with a binomial test.

- Mean change in the Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ) score from baseline to 13 weeks after the study procedure.

  The mean change in the MiniRQLQ score from baseline to 13 weeks will be tested using a paired t-test for a significant decrease greater than the MCID.
- Device-related and procedure-related serious adverse events through 13 weeks

  The proportions of serious device-related adverse events through 13 weeks will be calculated along with the 95% confidence interval.

6.12 Other Outcome Measures Analyses

Additional outcome measures will be collected for information and hypothesis generating purposes. The primary analysis methods will be descriptive and exploratory and presented by evaluation to more completely understand the time course of treatment effect. Measures will be summarized using frequencies and percentages for categorical measures and mean, median, standard deviation, minimum and maximum for continuous factors. Confidence intervals will be included where appropriate. Statistical comparisons will either not be performed or used for information purposes. Proportions may be compared using exact tests or chi-square tests. Continuous outcomes may be compared using t-tests, ANOVA or nonparametric equivalents. Repeated measures ANOVA or mixed effects modeling may be used for longitudinal analysis across evaluations.

Other outcome measures include:

- Nasal Assessment - The visual physical and endoscopic assessment factors will be summarized to include frequency and percentage of responses in each category for each component of the nasal assessment at baseline, just prior to treatment, immediately after treatment, and at 3 months after the procedure.
- Visual analog scale (VAS) for pain - Summary will include mean VAS pain scores assessed posttreatment and at 3 months.
- rTNSS - The rTNSS and its individual components will be subject to multiple summary methods and analyses including the:
  - Mean and mean change from baseline at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
  - Mean, mean change from baseline, and response distribution of the 4 components of the rTNSS (rhinorrhea, nasal congestion, nasal itching, and sneezing) at baseline and the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.

- Proportion of responders based on 30% improvement in rTNSS at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.

- Other rhinitis symptoms (cough and postnasal drip) - Mean, mean change from baseline, and distribution of the 4 response categories (0-3 points) at baseline and the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
- MiniRQLQ: The MiniRQLQ and its individual components will be subject to multiple summary methods and analyses including the:
  - MiniRQLQ mean and mean change from baseline at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
  - MiniRQLQ domain scores (nose symptoms, eye symptoms, non-eye/nose symptoms, sleep problems, practical problems, activity limitations, and emotional function) at baseline and the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
- Participant satisfaction assessment - mean response for each of the 5 survey questions will be summarized at the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
- Change in amount of PRN medication use for chronic rhinitis symptoms - Proportions of participants reporting increase, decrease, or no change in medications being used for treatment of symptoms compared to use prior to the procedure will be summarized for the 3-, 6-, 12-, 24-, and 36-month follow-up evaluations.
- Medications - A listing of medications associated with relief or treatment of chronic rhinitis symptoms or associated with treatment of adverse events will be provided. Medication use by categories may also be presented as percentages of participants.

6.13 Safety Analysis

All adverse events will be analyzed for all participants. Adverse events will be coded using a custom Aerin Medical dictionary so that adverse events may be categorized for analysis at an appropriate level of detail. Listings will be provided to detail individual events. The number of participants, number of AEs, and the proportion of participants reporting each AE will be summarized. Seriousness and severity of AEs and their relationship to the device and procedure will be summarized. A time course of adverse events will be presented. Any unexpected adverse device experiences or adverse events that occur at an unexpectedly high incidence rate will receive detailed analyses. Narratives will be presented for all deaths, serious adverse events, unexpected adverse device experiences, and participants withdrawn due to an adverse event.

6.14 Extension Phase Analysis

The extension phase analyses will be similar to those detailed above with a particular emphasis on the summarization of all adverse events occurring throughout the entire

study and the maintenance of the treatment effect over time. Missing data analyses and imputation will not be performed on data collected during the extension phase.

6.15 Standard Methods of Report

Summary descriptive statistics including means, medians, standard deviations and histograms for continuous measures, and frequencies and percentages for categorical outcomes will be presented for all variables of interest. Outcome measures (primary, secondary, and informational) will be presented by follow-up.

7.0 Adverse Events and Product Complaints

7.1 Adverse Events

Adverse events (AEs) may occur during the treatment phase or during the follow-up phase. Adverse events occurring after the baseline assessment but before the treatment procedure will be documented in the participant's medical record but will not count as related to the study device or procedure.

7.1.1 Definitions

Following are definitions associated with adverse events:

Adverse Event (AE) - any untoward medical occurrence, unintended disease or injury, or untoward clinical sign or symptom (including an abnormal laboratory finding), in subjects users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated (ISO 14155).

Serious Adverse Event (SAE) - an adverse event that led to any of the following (ISO 14155):

a) Death,

b) Serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:

   1) a life-threating illness or injury, or

   2) a permanent impairment of a body structure or a body function including chronic disease, or

   3) in-patient or prolonged hospitalization, or

   4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,

c) fetal distress, fetal death, or a congenital abnormality, or birth defect including physical or mental impairment

Note: Planned hospitalization for a pre-exiting condition, or a procedure required by the protocol, without serious deterioration in health, is not considered a serious adverse event.

Adverse Device Effect (ADE) - Adverse event related to the use of an investigational medical device.

Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. This definition also includes any event resulting from use error or from intentional misuse of the investigational medical device (ISO 14155).

Serious Adverse Device Effect (SADE) - an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event (ISO 14155)

Unanticipated (Serious) Adverse Device Effect (UADE or USADE) - any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.3(s)).

Relationship to device and procedure
The potential relationship of the event to the device or procedure:

- Not related

  An adverse event for which sufficient information exists to indicate that there is no causal connection between the event and the device or procedure. The adverse event is due to and readily explained by the participant's underlying disease state or is due to concomitant medication or therapy not related to the use of the device or the procedure. In addition, the adverse event may not follow a reasonable temporal sequence following the procedure.

- Unlikely

  The relationship with the use of the device or procedure seems not relevant and/or the adverse event can be reasonably explained by another cause, but additional information may be obtained.

- Possibly related

  There is a reasonable possibility that the adverse event may have been primarily caused by the device or procedure. The adverse event has a reasonable temporal relationship to the use of the device or the procedure and follows a known or expected response pattern to the device or procedure, but alternative etiology is equally or more likely compared to the potential relationship to the use of the device or the procedure.

- Probably related

  There is a reasonable probability that the adverse event may have been primarily caused by the device or procedure. The adverse event has a reasonable temporal relationship to the use of the device or the procedure and follows a known or expected response pattern to the device or procedure.

- Definitely related

  The adverse event has a strong causal relationship to the device or procedure. The adverse event follows a strong temporal relationship to the use of the device or the procedure, follows a known response pattern to the device or procedure, and cannot be reasonably explained by known characteristics of the participant's clinical state or other therapies.

Every effort should be made to determine the cause of each adverse event, because a judgment must be made as to the relationship to the device or procedure. If an investigator cannot assign a causality category the event will be considered possibly related for reporting and analysis.

NOTE: The occurrence of a diagnostic or elective surgical procedure for a pre-existing condition, unless the condition becomes more severe or increases in frequency, would not be considered procedure-related or device-related.

Intensity of adverse events:

- Mild

  The adverse event is noticeable to the participant but does not interfere with routine activity.

- Moderate

  The adverse event interferes with routine activity but responds to symptomatic therapy or rest.

- Severe

  The adverse event significantly limits the participant's ability to perform routine activities despite symptomatic therapy. The adverse event requires medical or surgical treatment or results in hospitalization.

7.1.2 Documentation and Reporting of Adverse Events

All adverse events will be monitored from the time of enrollment through study exit. All adverse events must be reported on the Adverse Event Report eCRF. A description of the event, including onset date, resolution date, action taken, and the outcome should be provided. All adverse events will be followed until they are adequately resolved or reach a chronic, stable state. If a participant reaches the 36-month follow-up visit and is experiencing a new or ongoing adverse event, the study sponsor should be contacted to discuss the need and/or

methods for continued surveillance of the event. Adverse events will be evaluated by the investigator and differentiated by:

- Seriousness
- Intensity (mild, moderate, severe)
- Causality (in relation to the device or procedure)
- Unexpectedness.

Signs and symptoms considered normal postprocedure recovery (eg, postprocedure pain, transient sensory symptoms, fever, postanesthesia symptoms) do not have to be reported as adverse events. If these events require treatment outside that which is considered normal, they should be reported as adverse events.

All adverse events classified as an Unanticipated Adverse Device Effect, Serious Adverse Device Effect, or Serious Adverse Event need to be reported to the Sponsor within 24 hours of learning of the event.

Sponsor Contact: Anais Laborde
Telephone: (650) 518-9624
email: alaborde@aerinmedical.com

Investigators must also report promptly all unanticipated problems to their IRB/EC involving risks to participants or others and report adverse events according to the local reporting requirements. Reporting instructions and contact information will be provided in the site's Regulatory Binder for this study.

7.2 Product Complaints

7.2.1 Definitions

Product Complaint - Any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of an Aerin product (medical device) after it is released for distribution [21 CFR 820.3(b)].

Complaint – written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, usability, safety or performance of a medical device that has been released from the organization's control or related to a service that affects the performance of such medical device. [ISO 13485:2016]

Reportable Complaint – Any product complaint that represents an event, which must be reported to a regulatory agency including:

- US FDA (21 CFR Part 803)
- A Competent Authority within the European Community or a Notified Body (MDD)
- The Canadian HPFB

- Any regulatory agency, within the country of distribution.

Device Deficiency – inadequacy of a medical device with respect to its identity, quality, durability, reliability , usability, safety or performance.

Note: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labeling. This definition includes device deficiencies related to the investigational medical device or the comparator (ISO 14155)

7.2.2 Documentation and Reporting of Complaints

All product complaints, deficiencies, and malfunctions associated with devices will be documented on the appropriate eCRF and/or communicated to Aerin within 24 hours of first becoming aware of the event.

8.0 Study Administration

This study will be conducted in accordance with elements of ICH E6 Good Clinical Practice, Abbreviated Requirements of 21 CFR 812 for nonsignificant risk device studies, ISO 14155, the Declaration of Helsinki, the Belmont Report, and any applicable regional or national regulations.

The study sponsor has the overall responsibility for the conduct of the study according to all applicable regulatory requirements. The study sponsor will have certain direct responsibilities and will delegate other responsibilities to the investigator and study site. The study sponsor and investigator will ensure that the study is conducted according to all applicable regulations. All personnel participating in the conduct of this study will be qualified by education and experience to perform their tasks.

The study sponsor, treating physician, or any person acting for or on behalf of a sponsor or investigator shall act in accordance the applicable standards, guidelines and regulations.

This study is funded by Aerin Medical. The Clinical Trial Agreement (CTA), mutually signed by the study site and Aerin Medical, describes the agreement between sponsor and site with respect to study financing.

8.1 Investigator Training

Site initiation training will occur prior to the first procedure at a site. Investigators will be trained on the treatment procedure and use the RhinAer Stylus and Aerin Console. All study staff will be trained, as necessary, to ensure compliance with the protocol and regulatory requirements, as well as to ensure accurate data collection. Site training will include a detailed review of this protocol, use of the EDC system, eCRF completion instructions, adverse event reporting, product handling and inventory, monitoring logistics, and regulatory requirements.

8.2 Study Monitoring

Study monitoring will be carried out in compliance with FDA regulations, ISO 14155, and GCP guidelines. The monitoring for this study will be carried out by

monitors qualified by experience and training who are Aerin Medical employees or individuals contracted by Aerin to conduct monitoring activities. The study monitors will oversee the conduct of the study and evaluate compliance with the protocol, any specific recommendations made by the site's IRB/EC, and the signed Investigator Agreement. During the study, phone contacts and site visits will be conducted to ensure protocol compliance. Monitoring will include verification the informed consent was properly obtained for all study participants, a review of the clinical records for accuracy and completeness, resolution of missing or inconsistent results, a review of source documents, and ensuring adverse events, protocol deviations and device usage are properly documented. The monitor will conduct source data verification by verifying eCRFs are consistent with source documents. The investigator will make available to the monitor for review the informed consent forms, source documents, and any other relevant records for all study participants at the site. The investigator and other site personnel will be accessible to the monitor during visits and sufficient time is provided to conduct the visits and address questions. If the monitor becomes aware of any deficiencies during the course of the study, the monitor will discuss with the sponsor and investigator to ensure compliance is maintained. A final close-out monitoring visit will occur when the study has been completed or terminated.

8.3 Documentation of Study Findings

8.3.1 Data Management

A secure EDC and data management system will be used for entry, storage, review, and management of study data. The system will use the Medrio EDC platform (Medrio, Inc. San Francisco, CA) and be compliant with applicable GCP and regulatory requirements. Investigators are responsible for accurate completion and timely submission of the data collected during the study. Sites will be trained in the use of the system for entering study data and uploading supporting documents and will be given access for this purpose. Data monitoring will be performed to identify missing data, verify data accuracy and ensure queries are resolved. Any data issues are to be promptly addressed with the investigator. Quality assurance procedures will be established to ensure that complete, accurate and timely data are submitted, protocol requirement are followed, and that complications, adverse events and adverse device effects are correctly reported and investigator as appropriate. The management and retention of these data will be compliant with applicable regulatory requirements.

8.3.2 Case Report Forms

Standardized eCRFs will be used at all participating study sites to collect complete and accurate records of the clinical data. All study data will be entered by study personnel through eCRFs into the electronic database for each participant enrolled in the study. A unique ID number will be assigned to each participant.

The following CRFs and log will be used in this study and submitted at the intervals outlined in Table 1:

- Screening Visit / Study Eligibility (01)
- Baseline Visit Demographics and Treatment History (02)
- Follow-up (03)
- rTNSS / Cough and Postnasal Drip (04)
- Procedure (05)
- Pain VAS - Patient form (06A)
- Pain VAS - Site (06B)
- Study Exit (07)
- Device Malfunction (08)
- Protocol Deviation (09)
- Adverse Event Report (10A) (reference AE Code List (10B))
- MiniRQLQ (11)
- Serious Adverse Event / Unanticipated Adverse Device Effect (12)
- Patient Satisfaction Survey (13)
- Medication Log (14)

Table 1. Schedule of case report forms and related materials.

Visit	Visit window (days)	CRF	Other
Screening / Baseline	n/a	01, 02, 04, 11, 14	Informed Consent Nasal assessment images†
Treatment Procedure	within 30 days of Baseline	05, 06A, 06B	Nasal assessment images†
13-Week office)	±14	03, 04, 06A, 06B, 11	Nasal assessment images†
6-Month (Remote)	±30	03, 04, 11, 13	
12-Month (Remote)	±30	03, 04, 11, 13	
24-Month (Remote)	±30	03, 04, 07, 11, 13	
As Needed	n/a	07, 08, 09, 10A, 12, 14	

†Transfer to USB flash drive and provide to Sponsor.

8.3.3 Investigator Responsibilities, Records, and Reports

Responsibilities

The investigator is responsible for ensuring that the study is conducted according to the protocol and all IRB/EC requirements. In addition, the investigator is responsible for obtaining participant's written authorization for disclosure and use of health information as required under the Health Insurance Portability and Accountability Act (HIPAA; 45 CFR Parts 160 and 164), or other documentation as required by the IRB/EC and national regulations.

Records

The investigator will maintain complete, accurate and current study records. Investigator records including:

1. Relevant communication that documents any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, or adverse event reporting, including that with the IRB/EC, the sponsor, the study monitors, other investigators, and regulatory agencies.
2. Device accountability records that will track device usage for all study participants. Information tracked will include date of receipt, lot or serial number, date of usage, participant ID and disposition of all study products, including the type and quantity of the product, the dates of their return, if applicable, the occurrence of any device malfunctions, and initials of study personnel conducting the device accountability.
3. Participant records, including the participant's informed consent form, case history, procedure dictation, adverse events, progress notes, follow-up evaluations, case report forms and all supporting documents, such as diagnostic studies.
4. Study Protocol, amendments, and documentation (dates and reasons) of any deviations from the protocol.
5. IRB/EC records, including original and ongoing study approvals, all correspondence, and the approved informed consent form.
6. IRB/EC membership list, FWA# as applicable, statement of compliance and written procedures pertaining to AE and protocol deviation reporting (if available).
7. Study agreement, curricula vitae of investigator(s), financial disclosure, signature authorization log (delegation of responsibility), protocol signature page, and patient screening/enrollment log.
8. Reports (including safety reports, progress reports and a final report from the investigator).
9. Any other records, as required by the IRB/EC and the sponsor.

Reports

Investigators are required to prepare and submit the following reports in a complete, accurate and timely fashion:

1. In the event of an adverse experience that is serious or unexpected, or which requires action by sponsor to prevent an unreasonable risk of substantial harm to public health, notice shall be given immediately (but in no event later than 24 hours after learning of such experience) by telephone, facsimile, or email to the Sponsor and the IRB/EC. Any notices made by telephone shall be confirmed in writing within 2 days of the initial notification. The site shall provide all associated documentation (eg, lab reports, death summary, operative reports, etc.) for each adverse experience.
2. Unexpected adverse device effects and serious adverse events should be reported to the sponsor within 24 hours of event discovery. If the adverse event is alarming, the investigator shall report the event immediately.
3. Investigators shall promptly report to the IRB/EC all changes in the research activity and all unanticipated problems involving risk to participants and others, and that he or she will not make any changes in the research without IRB/EC approval, except where necessary to eliminate apparent hazards to the participants.
4. Withdrawal of IRB/EC approval to the sponsor within 5 working days. The report will include a complete description of the reason that approval was withdrawn.
5. Progress reports must be submitted to the IRB/EC at regular intervals dictated by the IRB/EC but no less than annually.
6. A final report must be submitted to the IRB/EC within 3 months after 1) termination or completion of the study; or 2) the investigator's work on the study ceases.
7. Any deviation from the protocol to protect the life or physical well-being of a participant in an emergency is to be reported to the sponsor and IRB/EC no later than 5 working days after the emergency occurs. Deviations to the informed consent process (eg, use of study product without informed consent) must be reported to the Sponsor and the IRB/EC immediately but no later than 5 working days after the use occurs.
8. Other: upon request, the investigator will supply accurate, complete and current information about any aspect of the study to the sponsor.

8.3.4 Retention of Study Records

The sponsor must ensure that all study participant records are stored for at least 2 years after the later of the following 2 dates: the date on which the study is terminated or completed (all subjects through final follow-up), or the date that the records are no longer required by the study site record retention policy. To avoid error, the site should contact the sponsor prior to the destruction of study records to ensure that they no longer need to be retained. In addition, the sponsor should be contacted if the study site is acquired or shuts down so that arrangements can be made for the handling or transfer of study records.

8.3.5 Data Quality Assurance

The sponsor, or the sponsor's representative, may conduct audits at the study sites. Audits may include, but are not limited to, device supply, presence of required documents, the informed consent process, and comparison of eCRFs with source documents. The investigator agrees to participate with audits conducted at a reasonable time, in a reasonable manner.

8.3.6 Confidentiality

All information provided to investigators, IRBs/ECs, and generated in this study must be considered highly confidential and must not be disclosed to any persons not directly involved with the study without prior written permission from the sponsor. However, authorized regulatory officials and sponsor personnel (or their representatives) will be allowed full access to inspect and copy the records. All study products must be used solely in accordance with this protocol. Privacy and confidentiality of information about each participant shall be preserved in the reports and in any publication. Each participant in this study will be assigned a unique identifier. All data will be tracked, evaluated, and stored using only this unique identifier.

The study site will maintain a confidential list (paper or electronic) identifying all participants. This list will contain the assigned participant's unique identifier and name. The treating physician bears responsibility for keeping this list confidential. This list will not be provided to the study sponsor and is only to be used at the study site.

Monitors and auditors will have access to the study patient list and other personally identifying information of participants to ensure that data reported corresponds to the person who signed the informed consent form and the information contained in original source documents. Such personal identifying information may include, but is not limited to the participant's name, address, date of birth, gender, race and medical record number.

8.3.7 Publication Policies

The CTA mutually signed by the investigator(s) and Aerin Medical, defines and describes the nature of the study agreement. The data and results from this study are the sole property of Aerin Medical. Aerin Medical shall have the right to

access and use all data and results generated during the clinical investigations. Publication authorship will be established according to International Committee of Medical Journal Editors (ICMJE) guidelines and Aerin Medical policy. Clinical study design will be publicly disclosed on ClinicalTrials.gov, and summary results posted per FDAAA 801 requirements. Additionally, an investigator may only publish data generated by this trial in accordance with the terms of the CTA.

It is Aerin Medical's intent to encourage and facilitate the publications of scientifically important results, while simultaneously ensuring minimization of duplicative data publication and the priority publications of multicenter results ahead of single-center investigations.

Aerin Medical intends to provide research sites with a standardized study report containing aggregated site study data.

8.4 Study Suspension or Early Termination

The study can be suspended or discontinued at the discretion of the sponsor for reasons including, but not limited to, the following:

- Obtaining new scientific knowledge that shows that the study is no longer valid or necessary,
- Insufficient recruitment of patients,
- Unanticipated adverse device effect presenting an unreasonable risk to the patients,
- Persistent noncompliance with the protocol and/or IRB/EC or regulatory authority requirements.

If the study is discontinued or suspended prematurely, the sponsor shall promptly inform all participating study sites and treating physicians of the termination or suspension and the reason(s) for the termination or suspension. The IRB/EC shall also be informed promptly and provided with the reason(s) for the termination or suspension by the sponsor. The investigator shall promptly inform enrolled participants at his/her study site, if appropriate. Regulatory authorities and the personal physicians of the participants may also need to be informed if deemed necessary. All applicable study documents will be subject to the same retention policy as detailed in Section 8.3.4.

9.0 Ethics

9.1 Institutional Review Board/Ethics Committee

This study may not be initiated at a site until applicable Institutional Review Board/Ethics Committee, or regulatory authority approval/favorable opinion is obtained. The Study Protocol, all Study Protocol amendments, written study participant information, informed consent form, and any other appropriate study-related information must be reviewed and approved by the IRB/EC. Any additional requirements or conditions imposed by the IRB/EC or regulatory authority shall be followed, if appropriate.

To assure proper review and study oversight, the IRB/EC must comply with the responsibilities, functions, and records requirements defined in the federal regulations (21 CFR Part 56) or per their regulatory authority.

The investigator at each site is responsible for submitting the appropriate study documentation to the IRB/EC for review and approval in accordance with federal regulations. The investigator is responsible for providing accurate, complete, and current information to the IRB/EC throughout the course of the study.

9.2 Ethical Conduct of the Study

The study will be conducted in accordance with the protocol, Good Clinical Practice (GCP), and all applicable regulatory requirements governing clinical studies of marketed products. Compliance with these requirements also constitutes conformity with the ethical principles that have their origin in the Declaration of Helsinki and the rights, safety and well-being of study subjects shall be protected consistent with these principles.

The sponsor will promptly review all information relevant to the safety of the product that is received and comply with all regulatory device safety reporting requirements.

9.3 Participant Privacy

The privacy of participants in this study will be protected by all reasonable means. The investigator is responsible for study records at the study site and must only disclose information as provided for in the site's Authorization to Use and Disclose Health Information, or in accordance with EC policies and national regulations. Each participant must give permission for use and disclosure of their information by signing the Authorization to Use and Disclose Health Information or documents as required by the EC and/or regulatory authority. This form may be a separate document from the informed consent form, or it may be contained within or as an addendum to the informed consent form. Although the sponsor is not a covered entity under HIPAA, access to study records, particularly participant information, will be strictly limited by the sponsor to the investigator, the sponsor's clinical research personnel, authorized representatives of the sponsor and the FDA under applicable federal regulations or other regulatory authority as required per national regulations. No public reporting or publications of the results of this study will contain identifiable references to individual participants in the study.

9.4 Participant Reimbursement

Participants will be reimbursed for their time for completing questionnaires as allowed by the IRB/EC and study site policies. Participants will not be reimbursed for questionnaires not completed.

9.5 Participant Insurance

It is the responsibility of the sponsor to provide insurance covering the cost of treatment of participants in the event of clinical-investigation-related injuries, in accordance with the national regulations, as applicable.

9.6 Participant Withdrawal

Participants may withdraw from the study at any time for any reason without impact to their future medical care at the study site. In addition, the investigator may withdraw a participant from the study, if in the investigator's opinion, it is not in the best interest of the participant to continue in the study. Any participant withdrawing from the study for any reason will continue to receive medically necessary follow-up care as determined by the investigator. Every attempt should be made to follow a participant withdrawing either because they failed to obtain a desired effect or suffered an adverse event.

When a participant chooses to withdraw, the investigator and study coordinator will make all possible efforts to collect and report the final visit observations. If the investigator has made 3 documented attempts to contact the participant and received no response, the participant may be considered to be lost to follow-up. A participant who misses a study visit but attends a subsequent visit will no longer be considered lost to follow-up. All reasons for withdrawals and documentation will be recorded in source documentation and the appropriate case report form. In addition, within the informed consent process, participants will be asked to provide consent for the study staff to contact them by mail or phone to follow up on safety-related issues as appropriate.

9.7 Protocol Modifications

This protocol shall not be amended without the approval of the sponsor. The sponsor may amend the protocol to clarify study procedures or to implement changes to the protocol that do not affect the validity of the data; the risk to benefit ratio; the scientific soundness of the protocol; or the rights, safety, or welfare of the participants. All modifications must be reviewed and approved by the IRB/EC at each study site, or a central IRB before implementation.

9.8 Protocol Adherence and Deviations

9.8.1 Definition

Deviation – instance of failure to follow, intentionally or unintentionally, the requirements of the protocol (ISO 14155).

9.8.2 Documentation and Reporting of Deviations

The investigator(s) agree to conduct the study in accordance with this protocol. An investigator must not make any changes in the study without first receiving approval in writing from the IRB/EC, except when necessary to eliminate apparent immediate hazards to a participant. Investigators will also adhere to procedures for reporting study deviations to their IRB/EC in accordance with their specific IRB/EC reporting policies and procedures. Deviations will also be reported to the regulatory authority as required per national regulations.

Deviations must be reported to the sponsor regardless of whether medically justifiable, pre-approved, or performed to protect the participant in an emergency. The investigator will document and explain the reason for the

deviation. Participant-specific deviations will be reported using the Protocol Deviation eCRF.

10.0 References

1. Quillen DM, Feller DB. Diagnosing rhinitis: allergic vs. nonallergic. *Am Fam Physician* 2006;73:1583-90.
2. Wallace DV, Dykewicz MS, Bernstein DI, et al. The diagnosis and management of rhinitis: an updated practice parameter. *J Allergy Clin Immunol* 2008;122:S1-84.
3. Dahl R, Mygind N. Anatomy, physiology and function of the nasal cavities in health and disease. *Adv Drug Deliv Rev* 1998;29:3-12.
4. Rogers DF. Airway goblet cells: responsive and adaptable front-line defenders. *Eur Respir J* 1994;7:1690-706.
5. Schroer B, Pien LC. Nonallergic rhinitis: common problem, chronic symptoms. *Cleve Clin J Med* 2012;79:285-93.
6. Greiner AN, Meltzer EO. Overview of the treatment of allergic rhinitis and nonallergic rhinopathy. *Proc Am Thorac Soc* 2011;8:121-31.
7. Halderman A, Sindwani R. Surgical management of vasomotor rhinitis: a systematic review. *Am J Rhinol Allergy* 2015;29:128-34.
8. Kirtane MV, Rajaram D, Merchant SN. Transnasal approach to the vidian nerve: anatomical considerations. *J Postgrad Med* 1984;30:210-3.
9. Arun GN, Sanu MP, Mohan M, Aparna TS, Afroze KHM. Effectiveness of endoscopic posterior nasal neurectomy for the treatment of intractable rhinitis. *Romanian J Rhinology* 2017;7:85-90.
10. Hwang PH, Lin B, Weiss R, Atkins J, Johnson J. Cryosurgical posterior nasal tissue ablation for the treatment of rhinitis. *Int Forum Allergy Rhinol* 2017;7:952-6.
11. Hytonen ML, Back LJ, Malmivaara AV, Roine RP. Radiofrequency thermal ablation for patients with nasal symptoms: a systematic review of effectiveness and complications. *Eur Arch Otorhinolaryngol* 2009;266(8):1257-1266.
12. Sapci T, Sahin B, Karavus A, Akbulut UG. (2003). Comparison of the effects of radiofrequency tissue ablation, CO2 laser ablation, and partial turbinectomy applications on nasal mucociliary functions. *Laryngoscope* 2003;113(3):514-519.
13. Jacobowitz O, Driver M, Ephrat M. In-office treatment of nasal valve obstruction using a novel, bipolar radiofrequency device. *Laryngoscope Investig Otolaryngol* 2019;4(2):211-217.
14. Scott J, Huskisson EC. Graphic representation of pain. *Pain* 1976;2:175-184.
15. Downie SR, Andersson M, Rimmer J, et al. Symptoms of persistent allergic rhinitis during a full calendar year in house dust mite-sensitive subjects. *Allergy* 2004;59(4):406-414.

16. US Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research. Allergic Rhinitis: Developing Drug Products for Treatment; Guidance for Industry. September 2018. Accessed April 1, 2020. https://www.fda.gov/media/71158/download

17. US Department of Health and Human Services; Food and Drug Administration; Center for Drug Evaluation and Research. Nonallergic Rhinitis: Developing Drug Products for Treatment; Guidance for Industry. September 2018. Accessed April 1, 2020. https://www.fda.gov/media/95943/download

18. Barnes ML, Vaidyanathan S, Williamson PA, Lipworth BJ. The minimal clinically important difference in allergic rhinitis. *Clin Exp Allergy* 2010;40:242-50.

19. Glacy J, Putnam K, Godfrey S, et al. Treatments for Seasonal Allergic Rhinitis. Comparative Effectiveness Review No. 120. (Prepared by the Blue Cross and Blue Shield Association Technology Evaluation Center Evidence-based Practice Center under Contract No. 290-2007-10058-I.). In: Quality AfHRa, ed. AHRQ Publication No. 13-EHC098-EF2013.

20. Meltzer EO, Wallace D, Dykewicz M, Shneyer L. Minimal Clinically Important Difference (MCID) in Allergic Rhinitis: Agency for Healthcare Research and Quality or Anchor-Based Thresholds? *J Allergy Clin Immunol Pract* 2016;4:682-8.e6.

21. Brixner D, Meltzer EO, Morland K, Carroll CA, Munzel U, Lipworth BJ. Implication of Alternative Minimal Clinically Important Difference Threshold Estimation Methods on Technology Assessment. *Int J Technol Assess Health Care* 2016;32:371-5.

22. Pfaar O, Demoly P. Gerth van Wijk R, et al. Recommendations for the standardization of clinical outcomes used in allergen immunotherapy trials for allergic rhinoconjunctivitis: an EAACI Position Paper. *Allergy* 2014;69(7):854-867.

23. Juniper EF, Guyatt GH. Development and testing of a new measure of health status for clinical trials in rhinoconjunctivitis. *Clin Exp Allergy* 1991;21(1):77-83.

24. Juniper EF, Thompson AK, Ferrie PJ, Roberts JN. Validation of the standardized version of the Rhinoconjunctivitis Quality of Life Questionnaire. *J Allergy Clin Immunol* 1999;104:364–369.

25. Juniper EF, Thompson AK, Ferrie PJ, Roberts JN. Development and validation of the Mini Rhinoconjunctivitis Quality of Life Questionnaire. *Clin Exp Allergy* 2000;30(1):132-140.

26. van Oene CM, van Reij EJ, Sprangers MA, Fokkens WJ. Quality-assessment of disease-specific quality of life questionnaires for rhinitis and rhinosinusitis: a systematic review. *Allergy* 2007;62(12):1359-1371.

27. Segboer CL, Terreehorst I, Gevorgyan A, Hellings PW, van Drunen CM, Fokkens WJ. Quality of life is significantly impaired in nonallergic rhinitis patients. *Allergy* 2018;73(5):1094-1100.

28. Juniper EF, Guyatt GH, Griffith LE, Ferrie PJ. Interpretation of rhinoconjunctivitis quality of life questionnaire data. *J Allergy Clin Immunol* 1996;98(4):843-845.

29. Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). American Thoracic Society. Accessed April 1, 2020. https://www.thoracic.org/members/assemblies/assemblies/srn/questionaires/rqlq.php

30. Turner D, Schunemann HJ, Griffith LE, et al. Using the entire cohort in the receiver operating characteristic analysis maximizes precision of the minimal important difference. *J Clin Epidemiol* 2009;62:374–379.

31. Barnes M, Vaidyanathan S, Williamson P, Lipworth B. The minimal clinically important difference in allergic rhinitis. *Clin Exp Allergy* 2009;40:242-250.