SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Proximal Hypoglossal Nerve Stimulation for Obstructive Sleep Apnea

Device Trade Name: aura6000™ system

Device Product code: MNQ

Applicant's Name and Address: Livanova USA, Inc.
100 Cyberonics Blvd.
Houston, TX 77058

Premarket Approval (PMA) Number: P250013

Date of FDA Notice of Approval: 3/18/2026

II. INDICATIONS FOR USE

The aura6000™ system is indicated for the reduction of apneas**,** hypopneas, or both in adult patients with moderate to severe obstructive sleep apnea (OSA), defined as an apnea-hypopnea index (AHI) of ≥ 15 and ≤ 65.

The aura6000™ system is intended for patients who failed, do not tolerate, or are ineligible to be treated with current standard of care treatments such as positive airway pressure (PAP), oral appliances (e.g. mandibular advancement device), or pharmacotherapy.

PAP failure is defined as an inability to eliminate OSA (AHI of greater than 15 despite PAP usage), and PAP intolerance is defined as:

- Inability to use PAP (greater than 5 nights per week of usage; usage defined as greater than 4 hours of use per night), or
- Unwillingness to use PAP (e.g., a patient returns the PAP system after attempting to use it).

III. CONTRAINDICATIONS

- Patients with combined central and mixed apnea-hyponea index greater than or equal to 25% of the total AHI.
- Patients with any functional or structural problem, medical illness condition that would prevent or interfere with implantation, activation or continued use of the aura6000™ system.

- Patients with an implantable device which may be susceptible to unintended interaction with the aura6000™ system. Consult the device manufacturer to assess the possibility of interaction.
- Women who are pregnant, planning to become pregnant or breastfeeding.
- Patients with any condition or procedure that has compromised neurological control of the upper airway.
- Patients who require magnetic resonance imaging (MRI):
  The generator and lead are MR unsafe devices. MRI exposure may result in dislodgement of implanted components and heating of the generator, lead, and/or electrodes, which may, in turn, cause tissue damage, damage to the device electronics, and/or voltage induction through the lead and generator. The aura6000™ system generator and lead must be explanted if an MRI is required.

  The Remote Control and Charger (RCC) and Charging Antenna (CA) are MR Unsafe devices. They are projectile hazards that must not be brought into the MR scanner room.

- Patients who require diathermy:
  Shortwave, microwave, and therapeutic ultrasound (hereafter referred to as diathermy) energy can be transferred through the stimulation system, causing damage to the implant and tissue damage, resulting in severe injury or death. Diathermy can also damage system components, resulting in loss of therapy and requiring additional surgery for explantation and replacement. Advise your patient to inform all their healthcare professionals that they must not be exposed to diathermy treatment. Injury to the patient or damage to the system components can occur during diathermy treatment:
  - Whether the system is on or off
  - Wherever diathermy is used on the body (not just over the system component)
  - Whether diathermy delivers heat or not

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the aura6000™ system instructions for use.

V. DEVICE DESCRIPTION AND INTENDED USE

The aura6000™ system is an implantable neurostimulator and lead used for proximal hypoglossal nerve stimulation (pHGNS). The system consists of five components: two implantable components – the aura6000™ Implantable Pulse Generator (IPG) and the lead (with cuff electrode) – and three external components: the Remote Control/Charger (RCC), Charging Antenna (CA), and the aura6000™ Clinical Manager (aCM), an external programming system, which is used to adjust stimulation settings. A description of the implanted and external components of the aura6000™ system is provided below.

A. Mechanism of Action

The aura6000™ system provides proximal hypoglossal neurostimulation (pHGNS) by unilaterally stimulating the proximal HGN, which innervates muscles of the tongue (**Figure 1**). By stimulating the HGN cyclically and continuously during sleep, it maintains the muscle tone of the tongue and upper airway so that obstruction of the airway is reduced or eliminated.

The therapy leverages the spatial organization of the hypoglossal nerve. Six contacts, helically arranged around the proximal hypoglossal nerve, each connected to an independent constant-current source, allow access and control of the tongue muscles. Cyclical tonic stimulation via multiple electrode contacts, with a maximum duty cycle of 50% (two electrode contacts utilized) and a minimum duty cycle of 16.7% (all six electrode contacts utilized) provides the flexibility to give tonus to the tongue in the desired position relative to the airway.

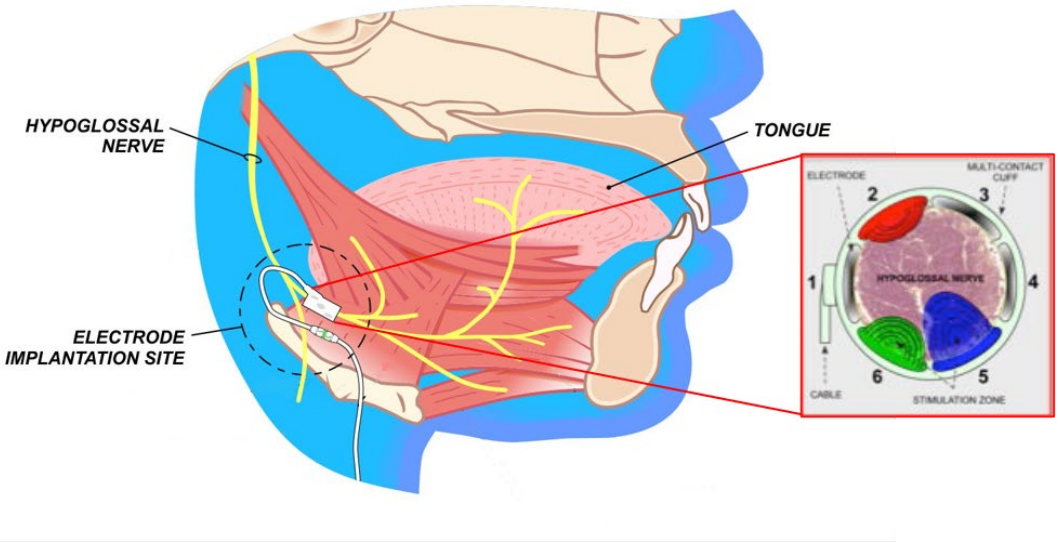

Figure 1. aura6000™ Lead Location on the Proximal Hypoglossal Nerve (pHGN)

In addition to the general system function and therapeutic mechanism, the following considerations apply to patient selection: A drug-induced sleep endoscopy (DISE) was not required for patient selection for proximal hypoglossal nerve stimulation (pHGNS). In clinical studies, patients with Complete Concentric Collapse (CCC) at the velum level were not excluded; however, CCC status was not systematically assessed or analyzed as a separate subgroup. As a result, the study population may have included individuals with CCC, but outcomes specific to this subgroup were not evaluated.

B. Model 100.0100 Implantable Pulse Generator (IPG)

The implantable pulse generator (IPG) is an implantable, multiprogrammable pulse generator that delivers electrical signals to the hypoglossal nerve. It is housed in a hermetically sealed titanium case and powered by a single rechargeable 50mAh Lithium-Ion battery with an expected battery life of up to 15 years (with nominal settings). It is recommended that the IPG be recharged at least every other day. Recharging typically takes less than 30 minutes but may require up to 90 minutes if the IPG is deeply depleted. The generator is placed under the skin of the upper chest, typically on the right side; however, left side placement is possible when required. The lead is typically attached to the right hypoglossal nerve in the neck. It runs under the skin to connect to the generator**.** Electrical signals are transmitted through the lead from the generator to the hypoglossal nerve. The lead and generator make up the implantable portion of the aura6000™ system. See **Figure 2.**

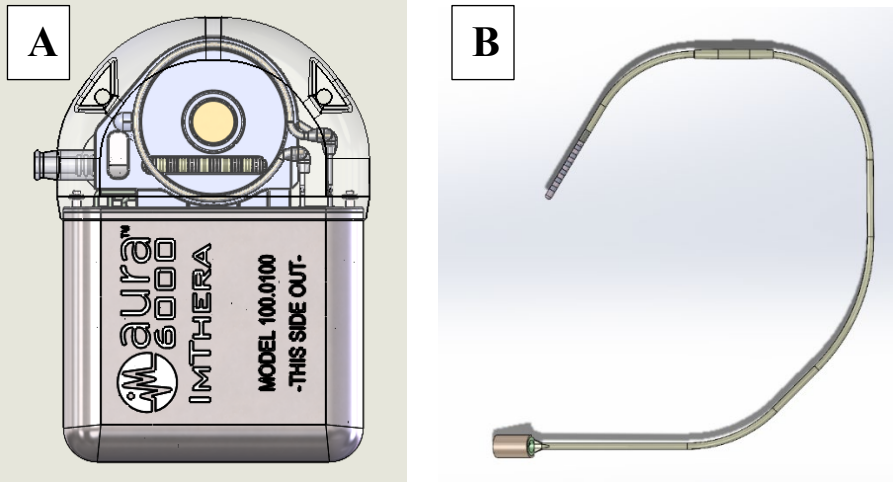

Figure 2. A) aura6000™ Implantable Pulse Generator (IPG) and B) aura6000™ Lead

IPG Intended Use

The aura6000™ IPG is intended to provide neurostimulation as a pulse generator with a built-in battery in conjunction with the lead for implantation in a subcutaneous pocket inferior to the collarbone over the pectoralis fascia, typically on the right side.

Table 1. aura6000™ IPG General Characteristics

Generator Model 100.0100	
Lead receptacle	1.5mm
Dimensions	47.5 x 33.3 x 9.4mm
Weight	16g
Battery Life	Approximately 15 years (with nominal settings)
Package Contents	• Generator* • Torque wrench • Suture sleeve
Material	• Case: Titanium • Header: Epoxy • Torque wrench: Stainless steel, Teflon, Polyethermide thermoplastic
* The aura6000™ generator is nonpyrogenic. ** No component of aura6000™ system is made with natural rubber latex.	

C. <u>Model 300.0100 (25cm) and Model 300.0200 (33cm) Lead</u>

The lead delivers the electrical signal from the generator to the proximal hypoglossal nerve and is insulated with silicone. It is designed using medical grade silicone tubing to insulate the MP35N multifilar conductor wires that terminate at the six (6) equally spaced platinum-iridium electrodes (approximately 50° radial spacing) inside the self-sizing nerve cuff which is

positioned around the proximal hypoglossal nerve. The lead, which is anchored to fascia using the suture sleeve, is available in 2 lengths to ensure optimal fit. The connector end of the lead is tunneled subcutaneously to the generator pocket. The lead is packaged with the torque wrench and suture sleeve.

Lead Intended Use
The aura6000™ Leads (25cm and 33cm) is intended to connect to the IPG on one end and securely placed around the proximal hypoglossal nerve on other end to allow the electrodes to make contact with the nerve to provide neurostimulation.

Table 2. aura6000™ Lead General Characteristics

Lead Model 300.0100/300.0200	
Electrode Type	Self-sizing cuff
Electrode Pattern	6 contacts, ~50° radial spacing
Electrode cuff inner	3.0mm
Connector	1.5mm diameter, 2.3mm contact spacing
Overall Length	25cm (Model 300.0100) 33cm (Model 300.0200)
Package Contents	• Lead* • Torque wrench • Suture sleeve
Material	• Lead Body Insulation: Silicone** • Lead Conductors: ETFE Coated MP35N and Silver • Electrode Connector: Platinum-Iridium • Electrode cuff: Silicone** • Connector Pin: MP35N, Platinum-Iridium and Polyurethance • Suture sleeve: Silicone**
* The aura6000™ Lead is nonpyrogenic. ** No component of aura6000™ system is made with natural rubber latex.	

D. Programming System

The external programming system includes the aura6000™ Clinical Manager (aCM), the Remote Control and Charger (RCC), and the Charging Antenna (CA). The aCM is a software application that allows the interrogation and programming of the aura6000™ generator. The aCM communicates with the generator via RCC and a USB cable.

Patients are provided with the RCC to start and stop a sleep session and a CA to charge the generator (**Figure 3**). The RCC also allows patients to adjust patient-specific therapy settings and determine implant status. The RCC battery powers the RCC and the CA.

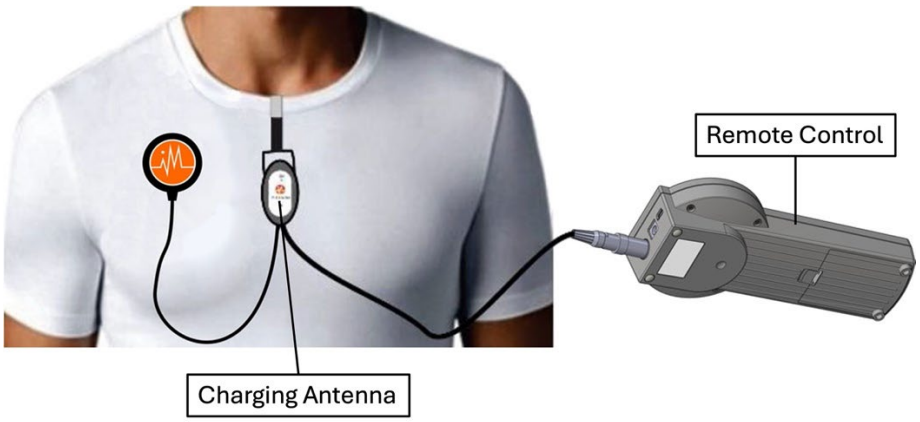

Figure 3. Patient IPG Charging Configuration

i. Model 700.0100 aura Clinical Manager (aCM) Intended Use

The aura Clinical Manager (aCM) is intended for use in conjunction with the implantable components to interrogate and program the IPG. It is intended for use by trained professionals in a hospital or healthcare setting. The aura6000™ Clinical Manager software application is operated on a computer running Microsoft Windows and is used to set the stimulation parameters of the IPG. The aCM communicates with the IPG via the RCC using a USB cable connection.

Key Functions:

- Surgical implant support: Verify system functionality through impedance testing and motor threshold level determination
- Therapy titration: Adjust stimulation parameters during polysomnography (PSG) sessions in both continuous and cyclical modes
- Patient follow-up: Modify comfort settings and download usage data
- System diagnostics: Interrogate device status, battery levels, and event logs

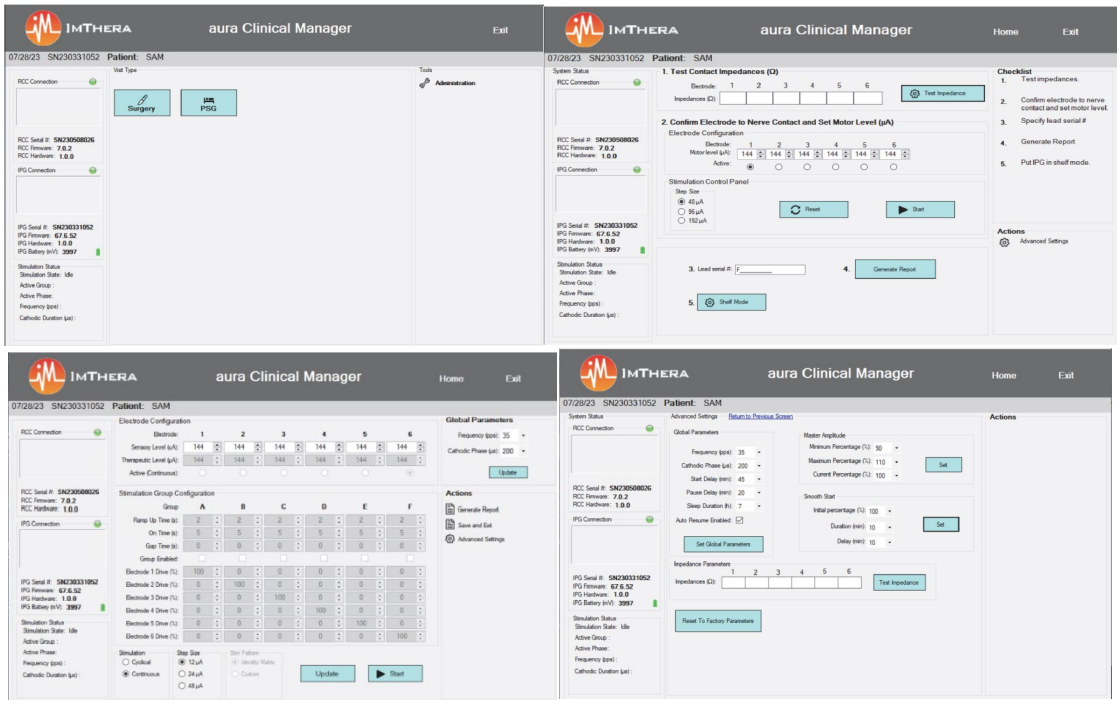

Figure 4. aCM Clinical Manager (Home, Surgery, PSG, and Advanced Settings Screens)

The aCM (**Figure 4**) is organized into a series of screens that correspond to the surgical implant procedure (Surgery screen), the titration procedure during which stimulation levels are defined (PSG screen), and the subject follow-up procedure during which comfort adjustments are made (Administration and Advanced Settings screens). The aCM can be used in conjunction with a Polysomnography (PSG) system to optimize therapy settings in real-time by visualizing the active contact being used (1 through 6) and the stimulation amplitude applied on that contact.

The aura6000™ system can deliver stimulation through any of the six contacts on the stimulation lead, using either individual contacts or user-defined contact groups. The system provides functionality to evaluate and configure stimulation using one or more contacts.

ii. Model 500.0300 Charging Antenna (CA) Intended Use

The CA is an external accessory that connects on the top surface of the RCC to charge the IPG. The CA establishes and maintains IPG-to-charging antenna (CA) alignment through a magnetic connection. The IPG must be charged at least every other day, with charging typically taking less than 30 though up to 90 minutes may be required if IPG is deeply discharged. The CA operates at 13.56 MHz and establishes magnetic alignment with the IPG through a magnetic connection. The charging distance is 5-10mm from the CA to the generator.

iii. Model 500.0100 Remote Control Charger (RCC) Intended Use

The Remote Control Charger (RCC) is intended to be used to interrogate and/or program the generator. The RCC is a handheld device housed in a plastic enclosure with a rechargeable battery pack. It allows patients to:

- Start/stop/pause stimulation during sleep sessions

- Charge the IPG (when used with the Charging Antenna)
- Adjust amplitude within physician-prescribed limits (Master Amplitude Control)
- Adjust patient preference settings including start delay, pause delay, and sleep duration
- Monitor system status including battery levels and therapy usage

The RCC communicates wirelessly with the IPG using MedRadio Band (401-406 MHz) at a distance up to 1.5 meters. The RCC also connects to the aCM via USB cable to enable physician programming of the IPG. The RCC battery powers both the RCC and the CA and is recharged by connecting to the provided wall power adapter.

Communication Interface

- Wireless Interface: RCC to IPG communication using CC1101 RF transceivers (MedRadio Band, 401-406 MHz)
- Inductive Interface: RCC charges IPG via CA at 13.56MHz
- USB Interface: RCC to aCM connection for physician programming
- Network Interface: aCM to LivaNova cloud resources for data uploads and software updates.

iv. Stimulation Parameters

The stimulation parameters (**Table 3**) are controlled by the IPG and programmed using the aura Clinical Manager (aCM). These parameters include pulse amplitude, frequency, and pulse width. The physician configures the stimulation parameters specific for each patient to provide optimal therapy during polysomnography (PSG) titration sessions. Using the RCC, the patient also has the ability to adjust the amplitude within physician-prescribed limits.

Table 3. aura6000™ system Stimulation Parameters

Parameter	Description	Available Range (step)	Default Setting
Waveform	Biphasic, charge-balanced waveform with anodic phase pulse amplitude equal to one-quarter of the cathodic phase pulse amplitude and anodic phase duration equal to four times the cathodic phase duration	N/A	N/A
Output Current (Amplitude)	Stimulation amplitude	0 to 1992 µA (12 µA steps)	Physician-determined during titration
Pulse Frequency	Pulse repetition rate	3, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, or 90pps	35 pps
Pulse Width (Cathodic Phase Duration)	Duration of the cathodic phase stimulation pulse	50 to 400 µs (25 µs steps)	200 µs
Number of Active Contacts	Number of electrode contacts delivering stimulation in sequence	2 to 6 contacts	Physician-determined (typically 2)
Duty Cycle	Percentage of time each contact is active	16.7% (6 contacts) to 50% (2 contacts)	Dependent upon number of contacts determined by physician
Start Delay	Time between therapy initiation and stimulation onset	0 to 60 min (15 min increments)	45 min
Pause Delay	Time between pause and therapy resumption	5, 10, 20, or 30min	20 min
Sleep Duration	Maximum therapy session duration	4 to 10 hours (1 hour increments)	7 hours

Figure 5 below provides a visual representation of the stimulation pulses delivered to the proximal HGN.

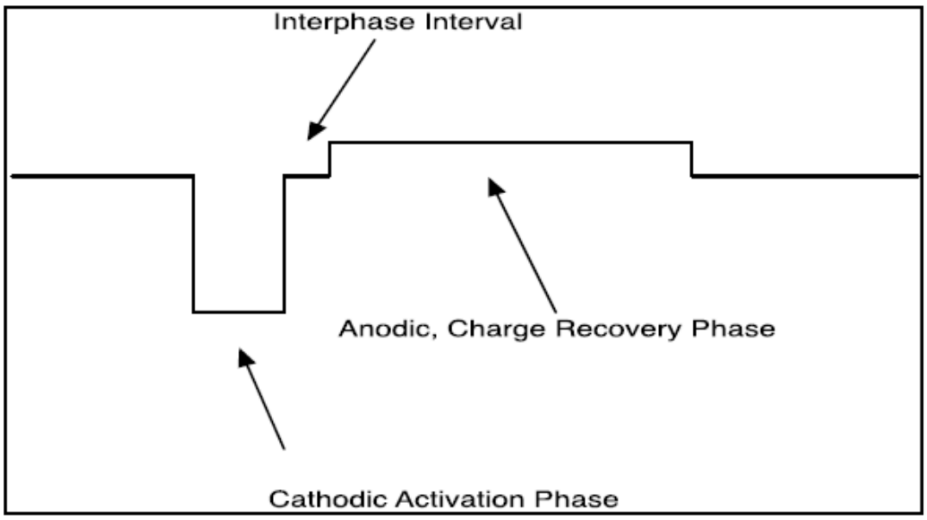

Figure 5. Visual Representation of Therapy Waveform

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative treatment options for patients with moderate to severe OSA include: lifestyle and behavioral approaches such as weight loss or positional therapy; positive airway pressure (PAP) therapies, oral appliances that work by temporarily advancing the mandible to prevent pharyngeal collapse during sleep; pharmacologic options such as glucagon-like peptide (GLP-1) receptor agonist, Tirzepatide, in patients with OSA and obesity, and upper-airway surgical procedures such as maxillomandibular advancement and uvulopalatopharyngoplasty, or bariatric surgery that treats obesity, which is known to worsen OSA symptoms.

Implantable hypoglossal nerve stimulation (HGNS) systems are also available treatment options for patients who decline or do not tolerate PAP therapy, including two FDA-approved devices - the Inspire® UAS System and the Nyxoah Genio® System.

Each alternative treatment has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the treatment method that best meets their needs.

VII. MARKETING HISTORY

The current aura6000™ system has not yet been marketed in any country. The system has not been marketed in the United States.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse events from hypoglossal nerve stimulation may include but are not limited to, the following. These events may result in hospitalization, prolongation of hospitalization, unanticipated surgery, tracheotomy, revision or replacement of system components, or death.

- **Medical/Surgical complications** – Infection; bleeding, hematoma, or seroma; scarring; excessive fibrotic tissue growth around the implanted device; temporary or permanent hypoglossal or other nerve damage resulting in paresis, facial nerve injury (marginal mandibular branch), paralysis or other dysfunction including difficulty or inability to swallow or speak; complications from anesthesia or extended procedure time; persistent pain at the implant site; allergic or immune system response to the implanted materials; and component migration or erosion through the skin.
- **Device complications** – Lead migration, dislodgement, disconnection, fracture, insulation breakage or erosion; failure of generator components, battery, software, or telemetry; loss of electrical isolation, and generator migration or flipping.
- **Stimulation complications** – Paresthesia (tingling); tongue weakness or movement disturbance, discomfort, pain, or glossodynia (burning sensation); speech disorders, loss of therapeutic effect; extrahypoglossal stimulation; and worsening of OSA condition.

For the specific adverse events that occurred in these clinical studies, please see **Section X.B.viii**.

IX. SUMMARY OF NON-CLINICAL STUDIES

Nonclinical testing for the aura6000™ system encompassed a range of evaluations, including bench testing of the device, biocompatibility, sterilization, packaging, shelf-life, software and cybersecurity assessments, electrical safety, electromagnetic compatibility, mechanical, human factors, and animal studies. These tests were conducted in accordance with design specifications, as well as relevant standards and guidance documents. A summary of the results for each test is provided below.

A. aura6000™ Implantable Pulse Generator (IPG) Testing (model 100.0100)

Table 4 presents high-level summary results of the aura6000™ IPG testing, with information regarding the test, purpose, applicable acceptance criteria and results. Beyond the testing summarized in **Table 4**, the IPG design was also reviewed for enhancements implemented to improve electrical isolation.

Summary of IPG Modifications

To address electrical isolation issues observed during the OSPREY study, modifications were made to the IPG design and manufacturing process. These included adjustments to the routing of the telemetry and charging coils as part of the isolation improvements. These changes were validated to ensure required electrical isolation. Subsequent verification testing confirmed that these modifications did not alter the electrical, thermal or functional performance of the device.

Table 4. aura6000™ Implantable Pulse Generator (IPG) Testing Summary

Test	Purpose	Acceptance Criteria	Results
Functional Testing	Verify IPG contact resistance	Contact resistance shall be less than 1 Ω.	PASS
	Verify IPG leakage current through dielectric strength testing after preconditioning	Dielectric strength testing at 25.2V after preconditioning shall result in less than 2.356 µA of current leakage. *(Following preconditioning by total immersion in 9 g/L saline solution for at least 10 days at 37°C ± 5°C)*	PASS
	Verify IPG leakage current of feedthrough pins after preconditioning	Feedthrough pins shall be insulated and shall allow a maximum leakage current of 2.356 µA between feedthrough pins and from any feedthrough pin to the case. *(Following preconditioning by total immersion in 9 g/L saline solution for at least 10 days at 37°C ± 5°C)*	PASS
	Verify IPG exposure to ultrasonic energy	No irreversible change per ISO 14708-1 Clause 22.1	PASS
	Verify setscrew torque	Set screw shall achieve ≥5 oz-in torque and the septum shall not dislodge after 10 cycles.	PASS
	Verify IPG withstand mechanical shock testing	IPG shall meet ISO 14708-1 Clause 23.7.	PASS
	Verify IPG withstand mechanical vibration testing	IPG shall meet ISO 14708-3 Clause 23.2.	PASS
Mechanical Design Verification Testing	Verify IPG predicted reliability by conducting mean time to failure (MTTF) calculations	IPG shall have predicted reliability of at least 90% at 5 years.	PASS
	Verify IPG strain relief tensile force	IPG header strain relief shall withstand a tensile force of 2.22 N.	PASS
	Verify IPG perpendicular force	IPG header shall withstand a perpendicular force to its planar surface of 133.5 N± 10 N for a period of ≥5 seconds.	PASS
	Verify IPG welding environment	IPG shall be welded in a 25% ± 5% Helium environment	PASS
	Verify IPG hermeticity	Helium leak rate shall be $<10^{-8}$ cc atm/s after pressurization.	PASS

Test	Purpose	Acceptance Criteria	Results
	Verify suture holes are free of functional damage after exposure to 13.3N	No visual appearance of cracks or broken material after applying 13.3 N axial force, 5 second duration	PASS
Product Shelf Life, Reliability Testing, and Storage Temperature Testing	Verify IPG product shelf life	Verify through accelerated aging, IPG meets its functional requirements after the labeled shelf life	PASS
	Verify IPG storage temperature	IPG shall endure storage temperature cycles (-10°C to 55°C) with no performance loss per ISO 14708-1 Section 26.2	PASS
	Verify IPG sterilization cycles	IPG shall endure 2x sterilization	PASS
	Verify IPG Temperature increase during maximum stimulation	Temperature increase shall be less than 2°C per ISO 14708-3 Clause 17.1	PASS
Resistance to X-Ray	Verify IPG withstands radiography	IPG program settings must remain at factory settings.	PASS
	Verify IPG x-ray identification	IPG shall have a unique radio-opaque marker or feature identifying the device when examined by x-ray.	PASS
Battery Testing	Verify IPG battery performance and longevity	Test 1: ≥ 22 cells (simulated real time) must allow single use per day projections.	PASS
		Test 2: ≥ 11 cells (accelerated stimulation and idle current) must allow projections using Test 2 data.	PASS
Atmospheric Pressure Testing	Verify IPG meets the international standards for atmospheric pressure	Meets the requirements of atmospheric pressure per ISO 14708-1 Clause 25.1	PASS
Electromagnetic Compatibility (EMC) Testing	Verify the IPG meets international standards for electromagnetic compatibility	Meets requirements of electromagnetic compatibility per ISO 14708-1/-3 Clause 27 and EN 45502-1	PASS
Defibrillation Protections	Verify the IPG meets international standards for defibrillation protection	Meets requirements of defibrillation protection requirements per ISO 14708-1 Clause 20.2	PASS
Electrocautery Resistance	Verify the IPG meets internal standards for resistance to electrocautery	Meets requirements of resistance to electrocautery per ISO 14708-1 Clause 21.1	PASS

B. aura6000™ Lead Testing (models 300.0100, and 300.0200)

Table 5 presents high-level summary results of the aura6000™ Lead testing, with information regarding the test, purpose, applicable acceptance criteria and results. Additional analyses were conducted to evaluate safety aspects related to the stimulation configuration.

Summary of Monopolar Stimulation Analysis
An analysis was performed to characterize the potential for off-target effects from current spread associated with pHGNS, a monopolar approach to stimulation of the hypoglossal nerve used in the treatment of OSA with the aura6000™ system. This evaluation included anatomical review of structures adjacent to the proximal hypoglossal nerve, computational modeling of electric field distribution including worst-case proximity modeling this adjacency, and assessment of stimulation-related adverse events observed during clinical use. Modeling showed that adjacent nerves would require currents substantially higher than the maximum output of the device to reach activation thresholds, indicating a low likelihood of unintended stimulation. Clinical observations were consistent with this finding, with no serious adverse events attributed to activation of off-target structures.

Table 5. aura6000™ Lead Testing Summary

Test	Purpose	Acceptance Criteria	Results
Tensile Load Testing	Verify the lead tensile force	Cuff electrode shall withstand a tensile force of up to 5 N with no loss of performance. *(Following preconditioning by total immersion in 9 g/L saline solution for at least 10 days at 37°C ± 5°C)*	PASS
Fatigue Testing	Verify the lead connector flexural fatigue	The lead connector shall withstand 82,000 flex cycles without conductor fracture per BS EN 45502-1: 2015 Section 23.5; BS EN 45502-2-1: 2003 Section 23.5	PASS
	Verify the lead body flexural fatigue	After ≥ 235,000 cycles, pass visual inspection per specification. No damage to the coil wires or tubing and pass electrical test per BS EN 45502-1: 2015 Section 23.5; BS EN 45502-2-1: 2003 Section 23.5	PASS
	Verify the lead transition flex fatigue	Must withstand ≥ 82,000 cycles, and lower bound of the one-sided 95/95 tolerance interval must be > 82,000 per BS EN 45502-1: 2015 Section 23.5; BS EN 45502-2-1: 2003 Section 23.5	PASS
Insertion and Extraction Testing	Verify the lead maximum insertion force	The lead shall require an insertion force of less than 10 N (2.2 lbf) to be fully inserted into the IPG header.	PASS

Test	Purpose	Acceptance Criteria	Results
	Verify the lead maximum extraction force	The lead shall require a maximum extraction force of less than 10 N (2.2 lbf) to be fully removed from the IPG header.	PASS
	Verify the lead minimum extraction force	The connector shall require a minimum of 10 N (2.2 lbf) to extract the lead from the IPG when the setscrew is engaged. Resistance measurement for each lead channel shall be < 20 ohms and no damage or component detachment present. Re-connection shall be possible without degradation in performance.	PASS
	Verify the lead withstands repeated insertions	All insertion and extraction requirements listed above must be met after 10 repeated insertion/withdrawal cycles.	PASS
Electrical Performance Testing	Verify the lead allowable leakage is minimized in dry conditions	Current leakage between contacts in dry conditions shall be < 10 µA at 100 VDC.	PASS
	Verify the lead allowable leakage is minimized in in-vivo conditions	Current leakage between an active contact and any other contact/saline shall be < 2 mA, (*Following preconditioning by total immersion in 9 g/L saline solution for at least 10 days at 37°C ± 5°C and testing at 100V)*	PASS
	Verify the lead contact-connector and disk electrode resistance	Resistance shall be < 20 Ω.	PASS
Resistance to X-Ray	Verify the lead resistance to x-ray	Cuff electrode shall withstand radiography with no loss of performance.	PASS
Product Shelf Life, Reliability Testing, and Storage Temperature Testing	Verify the lead product shelf life	Verify the lead meets its functional requirements after the labeled shelf life	PASS
	Verify the lead storage temperature	Lead shall endure 2x sterilization and storage temperature cycles (-10°C to 55°C) with no performance loss.	PASS
	Verify the lead sterilization cycles	Lead shall endure 2x sterilization and storage temperature cycles (-10°C to 55°C) with no performance loss.	PASS

Test	Purpose	Acceptance Criteria	Results
Corrosion Testing	Verify material integrity of the lead following exposure to simulated use conditions and environments.	No trace element changes between control samples and test articles. *(Following preconditioning by total immersion in 9 g/L saline solution for at least 10 days at 37°C ± 5°C)*	PASS
Atmospheric Pressure Testing	Verify the lead meets the international standards for atmospheric pressure	Meets the requirements of atmospheric pressure per ISO 14708-1 Clause 25.1	PASS
Electromagnetic Compatibility (EMC) Testing	Verify the lead meets international standards for electromagnetic compatibility	Meets requirements of electromagnetic compatibility per ISO 14708-1/-3 Clause 27 and EN 45502-1	PASS

C. <u>aura6000™ Charging Antenna (CA) (model 500.0300) and Remote Control and Charger (RCC) (model 500.0100) Testing</u>

Table 6 presents high-level summary results of the aura6000™ CA and RCC testing, with information regarding the test, purpose, applicable acceptance criteria and results.

Table 6. Charging Antenna (CA) and Remote Control and Charger (RCC) Testing Summary

Test	Purpose	Acceptance Criteria	Results
CA Storage Temp and Humidity Testing	Verify the CA maintains performance after exposure to storage temperature and humidity extremes.	CA shall meet performance requirements at storage temperatures between -10°C to 55°C and ≤ 95% humidity (non-condensing).	PASS
CA Cable Flex and Tensile Testing	Verify the CA pigtail flex performance	CA Pigtail shall withstand 730 flex cycles (90° total) with no loss of performance.	PASS
	Verify the CA pigtail tensile test	CA Pigtail shall withstand ≤ 4 lbf with no loss of performance.	PASS
CA design verification	Verify the assembled CA meets its design intent	CA shall contain a coil attached to a cable, amplifier and a magnet within the coil for recharging the IPG battery.	PASS
CA has ESD protection verification	Verify the CA meets its ESD and reliability requirements	CA electronics shall have a predicted reliability of at least 90% at 1 year.	PASS

Test	Purpose	Acceptance Criteria	Results
RCC Mechanical Performance Testing	Verify the RCC maintains performance after exposure to storage temperature and humidity extremes.	RCC shall meet performance requirements at storage temperatures between -10°C to 55°C and ≤ 95% humidity (non-condensing) and no physical damage shall be observed.	PASS
	Verify the RCC predicted reliability by conducting mean time to failure (MTTF) calculations	RCC shall have a predicted reliability of at least 90% at 1 year.	PASS
RCC and CA Electrical Safety Testing	Verify the RCC and CA meet international standards for electrical safety	Meet the requirements for basic safety and essential performance per IEC/EN 60601-1-11.	PASS
Electromagnetic Compatibility (EMC) Testing	Verify the RCC and CA meet international standards for emissions and immunity	Meets requirements of emissions and immunity per IEC 60601-1-2, Clause 7 & 8.	PASS

D. aura6000™ system Level Testing

Table 7 presents high-level summary results of the aura6000™ system level testing, with information regarding the test, purpose, applicable acceptance criteria and results.

Table 7. System Level Testing Summary

Test	Purpose	Acceptance Criteria	Results
IPG and Lead System Verification Testing	Verify the IPG and lead repeated insertions performance	Lead proximal connector shall exhibit no mechanical detachment or damage due to the insertion into or removal from the IPG. Resistance shall be < 20 Ω; lead shall require an insertion and extraction force of < 10 N.	PASS
	Verify the IPG and lead maximum extraction force	Lead shall exhibit maximum extraction force < 10 N.	PASS
	Verify the IPG and lead maximum insertion force	Lead shall exhibit insertion force < 10 N.	PASS
	Verify the IPG set screw secures lead	The torque wrench shall deliver 4 oz-in of torque and mates with the IPG set screw.	PASS

Test	Purpose	Acceptance Criteria	Results
	Verify the lead retention when set screw engaged	Connector shall exhibit ≥ 10 N of force to extract the lead from the IPG, no damage or detachment, resistance shall be < 20 Ω. Per ISO 14708 (section 23.6), re-connection shall be possible without a degradation in performance.	PASS
	Verify temperature rise of the IPG and lead while stimulating	IPG and lead electrode: The calculated CEM43 value ≤ 21 over 10 hour sleep session.	PASS
RCC and CA System Verification Testing	Verify the RCC and CA connector	CA shall securely attach to the RCC with a locking connector	PASS
	Verify the RCC and CA operating conditions (Temperature and Humidity)	RCC and CA shall endure operating conditions testing with no loss of performance. Functions at 5°C to 30°C and 15% to 85% humidity (non-condensing) and no physical damage observed.	PASS
IPG, RCC and CA Electrical Safety Testing	Verify the aura6000™ system meets standards for system heating while charging IPG	Meets requirements of system heating while charging IPG per ISO 14708-3 Clause 17.1 and IEC 60601-1 Clause 11.1.1.	PASS
Torque Wrench and Suture Sleeve Mechanical Performance Testing	Verify supplied torque wrench functionality	A torque wrench shall be provided with the IPG in order to provide a header/connector retention force of at least 10 N and the torque wrench shall have a torque limit of 4 oz-in ± 1 oz-in.	PASS
Suture Sleeve Verification Testing	Verify suture sleeve functionality	Suture sleeve shall allow fixation of Lead body to fascia without having sutures tied directly to the lead body.	PASS

E. Biocompatibility

The aura6000™ system, which includes the IPG Model 100.0100, Lead Models 300.0100 and 300.0200 (with implantable suture sleeve), CA Model 500.0300, and RCC Model 500.0100, has undergone biocompatibility and/or chemical characterization testing (**Table 8**). This testing and subsequent biological and toxicological risk assessments conducted for the device confirms compliance with the requirements of ISO 10993-1:2018, "*Biological evaluation of medical devices. Part 1: Evaluation and testing within a risk management process*" and the FDA Guidance document titled *"Guidance for Industry and Food and Drug Administration Staff: Use of International Standard ISO 10993-1, Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing Within a Risk Management Process,"*

issued on September 8, 2023, as well as ISO 14791:2019, "*Medical Devices – Application of risk management to medical devices*."

Table 8. Summary of aura6000™ system Biocompatibility Evaluation

Test	Device	Purpose	Results
Cytotoxicity ISO 10993-5	- IPG - Lead - RCC - CA	Evaluate the devices for potential cytotoxic effects.	Pass, non-cytotoxic
Sensitization ISO 10993-10	- IPG - Lead - RCC - CA	Evaluate the devices for the potential to cause delayed dermal contact sensitization.	Pass, non-sensitizing
Irritation/ Intracutaneous Reactivity ISO 10993-10	- IPG - Lead - RCC - CA	Evaluate the devices for the potential to cause local dermal irritation.	Pass, non-irritant
Material Mediated Pyrogenicity ISO 10993-11	- IPG - Lead	Evaluate the devices for inducing a pyrogenic response.	Pass, non-pyrogenic
Acute Systemic Toxicity ISO 10993-11	- IPG - Lead	Evaluate the devices for inducing a systemic toxicity from acute exposure.	Pass, non-toxic
Genotoxicity ISO 10993-3	- IPG - Lead	Evaluate the devices for mutagenic potential.	Pass, non-mutagenic
ISO Chemical Characterization of Materials ISO 10993-18	- IPG - Lead	Chemical characterization of extractable and leachable chemicals associated with the device.	All test samples met the acceptance criteria with MOS>1 or exposure levels <TTC Limit.
Implantation/ Subchronic Toxicity ISO 10993-11 ISO 10993-6	- IPG - Lead	Evaluate safety and local/systemic effects in one canine for 30 days.	Pass; No pathological changes in the hypoglossal nerves. Expected inflammatory response per ISO 10993-6
	- IPG - Lead	Evaluate safety and local/systemic effects in two canine for 12 months.	Pass; No systemic toxicity. Safe implantation with normal tissue response. Some telemetry issues are likely due to the animal model.

Test	Device	Purpose	Results
	- IPG - Lead	GLP study to evaluate safety and local effects of implantation and systemic toxicity: • 90-day cohort: 5 • 365-day cohort: 5	Pass; No significant adverse reactions. Inflammatory response at implant sites decreased over time, indicating normal healing. No pathological changes in nerves or systemic tissues at both the 90 and 365 days.

F. Particulate Testing

The acceptance criteria for particulates for both the IPG Model 100.0100 and Lead Models 300.0100 and 300.0200 successfully met requirements of ISO 14708-1:2014, Clause 14.2 and EN 45502-1:2015.

G. Sterilization, Packaging and Shelf-Life

i. **Sterilization**

The aura6000™ IPG Model 100.0100 and aura6000™ Lead Model 300.0100 and Model 3000.0200 are sterilized through 100% ethylene oxide (EO) to a minimum of 10^{-6} sterility assurance level (SAL). The sterilization process has been developed and validated per AAMI/ANSI/ISO/EN 11135-1:2014 "*Sterilization of Health Care Products – Ethylene Oxide – Part I: Requirements for development, validation and routine control of a sterilization process for medical devices.*"

The IPG and lead meets the requirements of ISO 10993-7 for the limit of toxic sterilant residuals. The sterilization validation demonstrates that the IPG, as well as the torque wrench and suture sleeve packaged with the IPG, meet the requirement that the devices are delivered sterile by EO per ISO 11135. The lead is packaged separately.

ii. Packaging and Shelf Life

The IPG Model 100.0100 and Leads Models 300.0100 and 300.0200 use polyethylene terephthalate glycol (PETG) trays with Tyvek lids packaged in a shelf box. The packaging meets the requirements of ISO 14708-1:2014 "*Implants for surgery – Active implantable medical devices – Part 1: General requirements for safety, marking and for information to be provided by the manufacturer*" and of ISO 11607-1 "*Packaging for Terminally Sterilized Medical Devices Part I: Requirements for Materials, Sterile Barrier Systems, and Packaging Systems*".
The sterile packaged IPG is labeled with a validated shelf life of 1 year based on the packaging date. The sterile packaged Leads (Models 300.0100 and 300.0200) are labeled with a validated shelf life of 2 years based on the packaging date. IPG and Lead testing demonstrated the sterile barrier system maintains integrity over time using accelerated and real time aging which supports the labeled shelf life periods.

The RCC and CA packaging underwent shipping and handling testing in accordance with ASTM D4169, demonstrating compliance with ISO 14708-1 requirements for non-sterile

external components. Shelf life is not defined for the RCC and CA as these are non-sterile components. The bench testing performed to date supports the validated minimum service life of components as shown in Table 9. The service life values do not imply explantation or replacement after specified time. For implantable components, continued clinical use is determined by device functionality and clinical judgment rather than elapsed time. For external components, service life references reflect expected use, environmental exposure and support considerations, and do not represent hard functional expiration dates.

Table 9. Summary of aura6000™ system Sterility, Shelf-Life and Service-Life

Device	Sterile/ Non-Sterile	Shelf-Life	Service-Life
Implantable Pulse Generator (IPG)	Sterile	1 year	At least 5 years
Lead(s)	Sterile	2 years	At least 5 years
Charging Antenna (CA)	Non-Sterile	Not applicable	At least 1 year
Remote Control Charger (RCC)	Non-Sterile	Not applicable	At least 1 year
aura Clinical Manager (aCM)	Non-Sterile	Not applicable	Not applicable

H. IPG and RCC Firmware and Hardware and aCM Software

Firmware and Hardware testing for the IPG Model 100.0100 and RCC Model 500.0100 and Software for aCM Model 700.0100 was conducted in accordance with FDA's guidance document "*Content of Premarket Submissions for Device Software Functions*", dated June 14, 2023. The Firmware and Hardware functions that relate to the whole system were tested as a system (e.g. charging of the IPG, communication protocol, etc.).

i. IPG and RCC Firmware and Hardware

The purpose of the automated and manual testing of the IPG Model 100.0100 and RCC Model 500.0100 Firmware and Hardware was to verify core features such as therapy delivery, IPG charging, RCC charging, IPG and RCC operating modes, communication protocols, power consumption, monitoring of basic system functionality, therapy controls, reporting status and displaying of information, pairing, and resetting of the RCC and IPG safety features and cybersecurity.

Verification activities including code reviews, unit module testing, integration testing and Firmware and Hardware verification testing were all conducted and met ANSI/AAMI/IEC 62304:2006+AMD1:2015 standards.

ii. aCM Software

The purpose of automated and manual testing of the aCM Model 700.0100 Software was to verify user interface, therapy controls, reporting status and displaying of information, pairing, and cybersecurity controls.

Verification activities including code reviews, unit module testing, integration testing and software verification testing were all conducted and met ANSI/AAMI/IEC 62304:2006 and AMD1:2015 standard and adhere to IEC 62304.

I. Cybersecurity

Security aspects of the aura6000™ system were designed using a risk-based approach and followed the guidelines provided in FDA Guidance Document "*Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions*", dated June 27, 2025.

Security activities were performed to identify and mitigate potential security vulnerabilities throughout the development and verification phase of the aura6000™ system, including penetration testing and verification of security design requirements. Verification of cybersecurity requirements associated with the IPG Model 100.0100 Firmware, RCC 300.0100 Firmware, and aCM Model 700.0100 Software was successful. The aura6000™ system meets the definition of a cyber device under Section 524B of the Federal Food, Drug, and Cosmetic Act, and cybersecurity risks were evaluated as part of the safety and effectiveness determination. Appropriate cybersecurity controls and labeling were provided to support reasonable assurance that the device and related systems are cybersecure.

J. Animal Studies

All studies have been conducted in compliance with Good Laboratory Practice (GLP) regulations in 21 CFR Part 58. **Table 10** presents high-level summary results of four animal studies evaluating the aura6000™ system in a canine model, including information on study objectives, number of subjects, duration of study and results.

Table 10. Canine Studies (includes aura6000™ IPG and Lead) Summary

Study Objectives	Number of Subjects	Duration	Results
Evaluate aura6000™ in vivo safety and performance in canines	5 canines	5 months	System implantation was safe, with one device-related AE (IPG flipping) requiring surgical intervention. No systemic toxicity. Electrical performance stable in 3 animals; 2 showed impedance variability.
Non-GLP study to demonstrate safe removal of chronically implanted lead from the hypoglossal nerve.	2 canines	12 weeks	Safe implantation & removal of cuff electrode with no complications. Swelling observed post-implant in two animals but resolved without significant impact on the health and welfare of the animals or the study itself.

K. Human Factors

The vast majority of the aura6000™ system user interface (including the generator, lead, CA, RCC, and the associated user workflows) is classified as "user interface of unknown provenance" and assessed under Annex C of IEC 62366-1:2015 as the user interface development predated the IEC 62366 usability standard. The remaining user interface updates (primarily involving the aCM) follow the usability engineering process per IEC 62366-1:2015 and FDA's 2016 Human Factors Guidance (*"Applying Human Factors and Usability Engineering to Medical Devices"*, issued on February 3, 2016).

This usability test approach is illustrated in **Figure 6**. Critical tasks were evaluated in 1 formative and 1 summative testing. The summative test was conducted with 16 actual users (Operating Room Support Specialists). This sample size was determined based on the 2016 FDA Human Factors Guidance. The test goal was to ensure no use errors create unacceptable risks. All criteria were met, and no use errors were identified to result in unacceptable risk, confirming the aura6000™ system meets user needs.

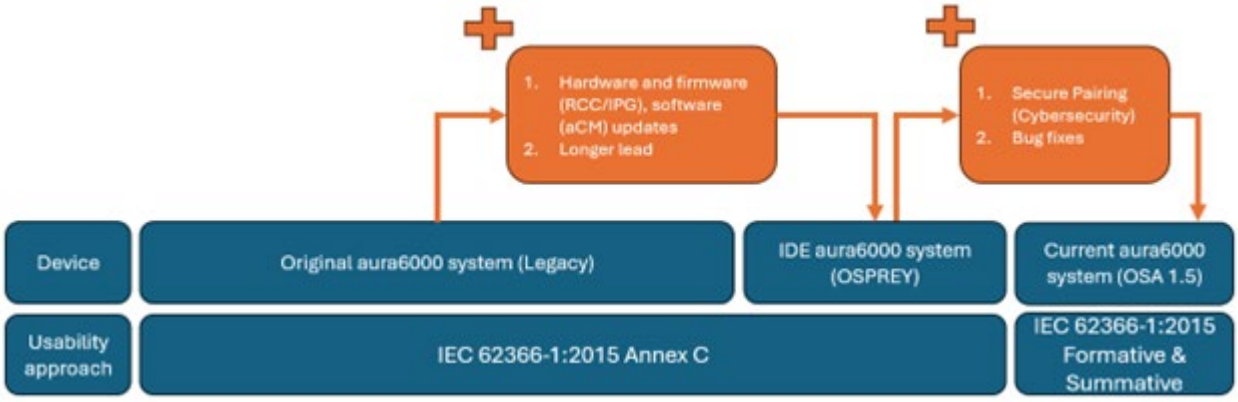

Figure 6: aura6000™ Development History and Usability Test Approach

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

A total of four (4) clinical studies, involving over 300 subjects treated with an iteration of the aura6000™ system, and over 240 within two randomized studies, provided data on the device's safety and effectiveness, with the maximum follow-up period extending up to 5 years. These included two feasibility studies and two randomized controlled trials (RCTs), collectively supporting the long-term safety and effectiveness of the system. The multi-center OSPREY pivotal RCT was conducted in the USA to establish evidence of safety and effectiveness of proximal hypoglossal nerve stimulation with the aura6000™ system as a potential therapeutic option for individuals with moderate to severe OSA who have failed or do not tolerate PAP therapy.

The feasibility and pivotal studies are summarized in **Table 11** and further discussed below.

Table 11. Summary of Clinical Studies on the aura6000™ system

Document Number	Title	Study Type	Primary Endpoint	Sample Size	Conclusion
REG-00411-01	THN Study #1 (THN1)	Early Feasibility study	Determine the safety, tolerability and preliminary efficacy of the HGNS up to 12 months	14	At 12 months AHI decreased by 53.6%, and 61.5% had ≥ 50% reduction in AHI (Sher criteria). ESS reduction exceeded MCID. The safety profile showed no unanticipated SAEs of concern and all AEs were fully resolved without permanent deficit. Technical issues during the trial were mostly related to the inability of subjects to consistently recharge their systems. These issues were addressed throughout the course of the study, and improved patient instructions coupled with improved charging capabilities were incorporated into the current iteration of the device.
G110125	THN Study #2 (THN2)	Feasibility study	At 12 months • Demonstrate that >50% of treated subjects were AHI responders (AHI < 20 and ≥ 50% reduction in AHI, Sher Criteria) • Demonstrate that > 50% of treated subjects	46	At 12 months, the AHI and ODI response rate was 32%, ESS score was -4.2 points (exceeding MCID). Subgroup analysis of baseline factors provided valuable insights for future patient selection. Device explant was performed in 5% of subjects (7/138). No UADEs or deaths. A total of 13 SAEs were deemed related, which

Document Number	Title	Study Type	Primary Endpoint	Sample Size	Conclusion
			achieve reduction in ODI ≥ 50% Secondary endpoints included QoL measurements		all resolved without sequalae. Suspension of therapy for 1 week at 6 months and 2 weeks at 12 months did not result in significant changes to AHI or ODI.
G140158	THN Study #3 (THN3)	RCT study, LTFU up to 5 years	At Month 4: RCT Phase Demonstrate that Treatment is superior to Control in 1) AHI RR (AHI < 20 and ≥ 50% reduction in AHI, Sher criteria), and 2) ODI RR (≥ 25% reduction in ODI) At 11 months of therapy (Month 12 for Treatment and Month 15 for Control): non-RCT phase Proportion of subjects in both groups that experience clinically meaningful long-term improvements at Month 12/15 versus Baseline AHI (≥ 50% responder rate required);	138	This RCT demonstrated superiority of THN therapy over a control group that underwent implant but no THN therapy, over a 4-month randomization period, as indicated by significantly improved measures of sleep-disordered breathing, daytime somnolence and quality of life. The beneficial effects were sustained for up to 5 years. Surgical intervention for device explants or revisions was performed at a rate of 5% per year through the first 4 years and increased to 7.7% in the fifth year. No deaths and no UADE were observed during the trial, and SAEs related to device, implant or procedure occurred in 1.4% of subjects. The annual rate of device revision or replacement remained below 5% through the first four years, increasing to 7.7% in year five. In total, 22 subjects

Document Number	Title	Study Type	Primary Endpoint	Sample Size	Conclusion
			ODI (≥ 50% responder rate required). Secondary endpoints included QoL measurements		underwent a device revision or replacement through Month 60.
G200365	OSPREY	Pivotal, RCT study	Primary efficacy endpoint is to demonstrate that the AHI responder rate of subjects with the device stimulation activated (Active Group) is statistically significantly higher than the AHI responder rate of subjects with the device stimulation not activated (Control Group) at M7 Secondary endpoints included ODI and QoL measurements	104	AHI Responder Rate (RR) in treatment group was statistically significantly greater than Control (58.2% vs 13.5% after 7 months), with the Active group AHI RR increasing to 64.6% after 13 months (12 months of treatment). All but 2 of the secondary endpoints found the Treatment superior to the Control. Surgical intervention for device explants or revisions was performed in 6% of Active subjects through 7 months (4/67). Procedure-related AEs observed in 41.3% of subjects. Through 7 months in the Active group, stimulation-related AEs observed in 19.4% of subjects and device-related AEs observed in 7.5% of subjects. No deaths and no UADEs were observed during the trial.
Abbreviations, ESS: Epworth Sleepiness Scale, LTFU: long-term follow-up, MCID: minimal clinically important difference, AHI: apnea hypopnea index, ODI: oxygen desaturation index, RR: responder rate, QoL: quality of life, UADE: unanticipated adverse device event,					

Document Number	Title	Study Type	Primary Endpoint	Sample Size	Conclusion
RCT: randomized controlled trial, Sher criteria defined as a reduction in AHI of at least 50% and a final AHI of 20 or less					

A. Clinical Studies

The THN1 Study (NCT01532180) was the first early feasibility study of the equivalent Legacy aura6000™ system. It was a single-center study conducted in Belgium, involving 14 subjects (14 implanted and 13 receiving stimulation therapy). The study demonstrated significant improvement and sustained effect in apnea hypopnea index (AHI) and oxygen desaturation index (ODI) over a 12-month period. At 12 months, the 13 subjects experienced a mean AHI reduction from 45.3 ± 17.6 events/hr at screening to 21.0 ± 16.5 events/hr, with a mean decrease of 24.2 ± 17.8 events/hr (53.6% improvement). Similarly, 10 subjects (76.9%) were found to be "responders" to the therapy at 12 months based on at least a 50% reduction in AHI. The safety profile did not show any unanticipated serious adverse events (SAEs), and all adverse events (AEs) were fully resolved without sequelae.

The THN2 Study, (NCT01796925) was a larger, multi-center study with 46 patients, which enrolled subjects in the USA and Europe. Fifteen of the 43 completers (34.9%) met the Sher criteria for AHI response at 6 months, and 12 of 38 (31.6%) completers at 12 months. The ODI results closely mirrored those of AHI. At 3, 6, and 12 months, the mean ODI decreased by approximately 9 points from baseline. Across all time points, 39.5% at 6 months and 31.6% at 12 months met the ODI responder criteria. Therapy suspension for 1 week at 6 months and 2 weeks at 12 months did not result in significant changes to AHI and ODI. Daytime sleepiness symptoms, measured by Epworth Severity Scale (ESS), showed clinically significant improvement from baseline during the treatment period, as evidenced by the lowering of mean scores by 3.7, 3.8 and 4.2 points, at Month 3, 6 and 12, respectively, well exceeded the minimal clinically important difference (MCID) of 2. Over the 12 months follow-up, no unanticipated adverse device effects (UADEs) or deaths were reported and 10 SAEs related to the device were reported. All device-related SAEs required surgical intervention or inpatient hospitalization, and resolved without sequalae after intervention.

The THN3 Study was a prospective, multi-center, randomized, controlled study. All subjects were implanted with the aura6000™ system and randomized to the Treatment (N= 92) or Control group (N=46) in a 2:1 ratio. Stimulation therapy was turned ON at Month 1 in the treatment group, and at Month 4 in the control group. All subjects received 11 months of pHGNS therapy with follow-up at Months 12 and 15, for Treatment and Control groups, respectively. The trial demonstrated superiority of THN therapy versus the Control group during the 4 month randomization period, where the responder rates for both AHI (Sher criteria) and ODI were significantly improved. Refer to **Table 12**.

Table 12: Co-Primary Effectiveness Endpoint – Treatment Response at Month 4, and Months 12/15 for THN3 Study

Endpoint	Treatment n/N (%)	Control n/N (%)	Absolute Difference [Treatment-Control] RR (95% CI)	Standardized Mean Difference [Treatment-Control] (95% CI)
M4 AHI RR	46/88 (52.3%)	9/46 (19.6%)	32.7 (15.2, 49.0)	0.725 (0.360, 1.163)
M4 ODI RR	55/85 (62.5%)	19/46 (41.3%)	21.2 (3.3, 38.1)	0.434 (0.070, 0.843)
Endpoint	**M11 Therapy Treatment and Control groups combined n/N (%)**		**Absolute Difference from Performance Goal of 50% (95% CI)**	
M12/15 AHI RR	59/138 (42.5%)		-7.5 (-16.0, 1.4)	- 0.151 (-0.330, 0.015)
M12/15 ODI RR	83/138 (60.4%)		+10.4 (1.6, 18.8)	0.214 (0.045, 0.402)
Abbreviations: AHI = Apnea-hypopnea index; ODI = Oxygen desaturation index; RR = Responder rate.				

The positive outcomes as assessed by AHI and ODI at Month 4 were maintained in available subjects through 5 years of follow up (**Table 13**).

Table 13. Change in AHI and ODI - Baseline to Month 60 Post-Implant for THN3 Study

Variable	Baseline	Month 12/15	Month 24	Month 36	Month 48	Month 60
AHI						
n	138	134	114	98	76	83
Mean (SD)	37.9 (9.8)	27.6 (21.1)	25.4 (18.6)	25.3 (20.1)	26.0 (21.5)	28.0 (20.7)
AHI Change from Baseline						
n	-	134	114	98	76	83
Mean (SD)		-10.1 (21.7)	-12.6 (19.9)	-12.5 (19.3)	-11.7 (21.3)	-8.7 (21.4)
p-value		< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.001
ODI						
n	138	134	114	98	76	83
Mean (SD)	37.3 (9.9)	27.2 (20.7)	26.6 (18.8)	27.4 (21.1)	29.5 (23.9)	31.0 (22.0)
ODI Change from Baseline						
n	-	134	114	98	76	83
Mean (SD)		-9.9 (20.7)	-10.9 (19.6)	-9.8 (19.9)	-7.5 (22.7)	-5.0 (21.8)
p-value		< 0.0001	< 0.0001	< 0.0001	< 0.001	< 0.05

Mean score difference from baseline at Month 4 for ESS, Functional Outcomes of Sleep Questionnaire (FOSQ), and EuroQol 5 Dimension (EQ-5D) questionnaires were all statistically significantly greater for the Treatment group versus Control group, thus fulfilling the secondary endpoint hypotheses (**Table 14**).

Table 14. Secondary Effectiveness Endpoints at Month 4: ESS, FOSQ and EQ-5D for THN3 Study

Endpoint	Treatment Mean (SD)	Control Mean (SD)	p-value
ESS	-4.5 (4.2)	-1.1 (3.5)	< 0.0001
FOSQ	2.5 (3.0)	1.1 (3.2)	0.0017
EQ-5D	5.3 (13.4)	0.6 (8.4)	0.0246
Abbreviations: ESS = Epworth Sleepiness Scale; FOSQ = Functional outcome of sleep questionnaire; EQ-5D = EuroQoL 5 Dimension.			

Quality of life indices, including ESS, FOSQ, EQ-5D Visual Analogue Scale (VAS) and the Snore Outcomes Survey (SOS) were also assessed at Months 12/15, 24, 36, 48, and 60. **Table 15** provides the differences at each follow-up visit compared to baseline. Across all follow-up visits, mean ESS, FOSQ, EQ-5D VAS and SOS values showed statistically significant improvements compared to baseline. These positive outcomes were sustained for up to 5 years post-implant in subjects who remained in the study.

Table 15. Quality of Life Endpoints Month 12/15 through Month 60 for THN3 Study

Variable	Baseline	Month 12/15	Month 24	Month 36	Month 48	Month 60
ESS						
n	133					
Mean ± SD	11.4 ± 4.8					
ESS Change from Baseline						
n	-	130	111	100	80	84
Mean ± SD		-4.8 ± 4.6	-5.1 ± 4.8	-5.3 ± 5.1	-5.2 ± 5.2	-5.0 ± 5.1
p-value		< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
FOSQ						
n	133					
Mean ± SD	14.9 ± 3.2					
FOSQ Change from Baseline						
n	-	130	112	100	80	85
Mean ± SD		3.1 ± 3.1	3.2 ± 3.3	3.5 ± 3.1	3.4 ± 3.2	3.5 ± 3.4
p-value		< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
EQ-5D VAS						
n	134					
Mean ± SD	78.4 ± 14.8					
EQ-5D VAS Change from Baseline						
n	-	131	112	101	80	86
Mean ± SD		4.3 ± 12.1	4.4 ± 12.4	5.2 ± 13.3	5.0 ± 16.0	5.8 ± 13.0
p-value		0.0001	0.0002	0.0002	0.0009	0.0001
SOS						
n		131				
Mean ± SD		28.9± 18.8				
SOS Change from Baseline						
n	-	110	91	79	63	69
Mean ± SD		36.6 ± 21.1	33.4 ± 21.5	33.1 ± 21.6	33.0 ± 23.4	29.2 ± 22.4
p-value		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Over the 11-month period, the majority of non-serious adverse events were classified as mild. Additionally, only two subjects (2 out of 138, 1.4%) experienced a serious adverse event. No deaths and no UADE were observed during the trial. Over the 12-month follow-up period, 2 out of 92 subjects (2.2%) required device revision or replacement within four months of implantation. The annual rate of device revision or replacement remained below 5% through the first four years, increasing to 7.7% in year five. In total, 22 subjects underwent a device revision or replacement through Month 60.

The three studies demonstrated long-term effectiveness and acceptable risk of the aura6000™ system in treating moderate to severe OSA through five years. They also provided data to support improvements in device design and patient/physician training, and to help determine criteria for patient selection for the pivotal trial.

B. OSPREY Pivotal Study titled "Treating Obstructive Sleep APnea using TaRgetEd HYpoglossal Neurostimulation: A Safety and Efficacy Trial for aura6000™ system

i. Study Design

There were 107 subjects implanted with the investigational device between 24 FEB 2022 and 01 APR 2024, where 104 subjects were included in the Intent-to-Treat (ITT) Population. There were 23 investigational sites with subject enrollment.

This study was a multi-center, open-label, prospective, randomized controlled trial using the aura6000™ system in adult patients with moderate to severe OSA who had failed or were unwilling to use PAP treatment. All subjects who signed the informed consent form (ICF) were screened for eligibility. If the subjects met all inclusion criteria and none of the exclusion criteria, they were qualified to be implanted with the aura6000™ IPG and Lead. All implanted subjects were randomized between 7 to 20 days post-implant, when they returned for the post-surgical visit, but prior to the Month 1 (M1) office visit and polysomnography (PSG) assessment. A qualified vendor provided independent scoring of PSGs throughout the study, and during the randomized phase of the study, was blinded to treatment assignments. Randomization was 2:1 in favor of stimulation therapy (Treatment Group). There was no allowance for crossover between treatment arms before Month 7 (M7). Note, all subjects were excluded from use of PAP or surgical treatments after enrollment.

The aura6000™ system can be adjusted to each subject's unique needs by testing different stimulation amplitudes across individual electrode contacts. This process aimed to identify the optimal contact settings to maximize tidal airflow, oxygenation (O_2 saturation), and overall sleep quality. The most effective configuration for each subject was then selected based on these parameters. This programming was made for the Treatment Group after M1 when therapy was turned ON for this group. Titration PSGs were based on the study schedule and subject needs.

ii. Inclusion and Exclusion Criteria

Subjects must have met all the following criteria to be considered for enrollment (**Table 16**).

Table 16. Inclusion Criteria

Criteria Number	Inclusion Criteria
1.	The patient is willing and capable of providing informed consent.
2.	The patient is at least 22 years of age.
3.	The patient is willing and capable of: • Using the remote control and charger to activate the therapy and charge the implant (assessed by the site), and • Completing all questionnaires.
4.	The patient is willing and capable of returning for all follow-up evaluations and sleep studies for the duration of the study.

Criteria Number	Inclusion Criteria
5.	The patient has documented diagnosis of moderate to severe OSA with an AHI of at least 15 using the AASM 2007 guideline for scoring hypopneas based on a nasal pressure drop of 30% or greater and a desaturation of >4%.
6.	The patient declines to use or does not tolerate PAP therapy.
7.	The patient expresses no difficulty with sleeping in unfamiliar environments and can do so without the use of drugs or medications.

Subjects who met any exclusion criteria were not eligible to be enrolled in the study (**Table 17)**.

Table 17. Exclusion Criteria

Criteria Number	Exclusion Criteria
1.	The patient is implanted with another active implantable device that could experience an unintended interaction with the aura6000™ system.
2.	The patient is enrolled in another clinical study that has not reached conclusion or may confound the endpoint of this study.
3.	The patient is dependent on or frequently taking medications (such as opioids, narcotics, or stimulants) that significantly alter consciousness, the pattern of respiration, sleep architecture, or with known effect on sleep-wake function or alertness.
4.	The patient has difficulty falling asleep and/or uses a hypnotic for insomnia more than twice a month.
5.	The patient has moderate to severe (or poorly controlled) respiratory disease (e.g. COPD such as emphysema, TB, chest wall disease, uncontrolled asthma, allergic rhinitis, etc.) or is on supplemental oxygen therapy for any reason to control the respiratory disease.
6.	The patient has one of the following: moderate to severe heart failure, in the assessment of the investigator, [NOTE: NYHA Class II or above], or a history of persistent atrial fibrillation, unstable angina, recent history of MI (<6m), severe cardiac arrhythmias, or uncontrolled systemic or pulmonary hypertension.
7.	The patient has neurological, neuromuscular, or neurodegenerative disorders (e.g. transient ischemic attack (TIA), cerebrovascular accident (CVA), Parkinson's, multiple sclerosis (MS), muscular dystrophy (MD), epilepsy, diagnosed memory dysfunction, etc.).
8.	The patient has other sleep disorders that, in the opinion of the Investigator, could confound functional assessment of sleepiness (e.g., narcolepsy, insomnia, etc.) or sleep movement disorders (e.g. Restless Leg Syndrome (RLS), Periodic Limb Movement (PLM) disorder) that may cause sleep disturbances unrelated to OSA.
9.	The patient has an active psychiatric condition that, in the opinion of the investigator, might interfere with the patient's compliance with the protocol,

Criteria Number	Exclusion Criteria
	or affect endpoints' assessment (e.g. depression, schizophrenia, bipolar disorder, etc.).
10.	The patient has an active systemic infection.
11	The patient has been admitted to rehabilitation for treatment of alcohol, tobacco, or recreational drug use within the last 12 months and/or has a history of habitual binge drinking. Must also be willing to refrain from alcohol use on the day of ALL PSGs.
12.	The patient is unwilling or unable to refrain from other OSA treatments including PAP, oral appliances, surgery, or medications, from enrollment through the completion of the study
13.	The patient has sleep hygiene behavior(s) that would substantially interfere with the study or its outcome assessment (e.g., shift work, sleeps less than 5 hours a night, psychophysiological insomnia, etc.).
14.	The patient has a body mass index (BMI) > 35 kg/m^2.
15	The patient exhibits clinical evidence of renal insufficiency, acute or chronic renal failure, or undergoing or expected to undergo dialysis in the future.
16.	The patient has a condition likely to require future MRI, diathermy or other procedure producing strong radio frequency (RF) fields.
17.	The patient is pregnant or planning to become pregnant between consent and the final Month 13 (M13) visit, must also be willing to use a contraception method during this time (pre-menopausal women only).
18.	The patient has another reason the Investigator feels (s)he is a poor candidate for participation in the study (e.g., prior radiation therapy for cancer treatment, pre- existing hypoglossal nerve damage, various palsies, cranio-facial or bony trauma, etc.).
19.	The patient requires the use of aspirin, non-steroidal anti-inflammatory drugs (NSAIDS) or anti-coagulant medications that cannot be safely stopped at least 3-7 days prior to the scheduled implant per the surgeon's clinical standard of care. Acetaminophen is permitted if needed.
20.	The patient has conditions causing chronic pain that may affect the subject's ability to sleep comfortably in the sleep lab (e.g. herniated discs, degenerative disc disease, sciatic nerve pain, etc.).
21.	The patient whose upper airway exam has a palatine or lingual tonsil grading system of 3 or 4, or HGN palsy.
22.	The patient has obstructive upper airway lesions (e.g. tumors, polyps, etc.), or severe septal deviation.
23.	The patient exhibits evidence of Cheyne-Stokes or periodic breathing.
24.	The patient has been diagnosed with central sleep apnea per the International Classification of Sleep Disorders 3rd Edition (ICSD-3) definition.
25.	Inability to obtain a repeatable AHI value (i.e., high variability in AHI >20) between screening home sleep tests (HSTs).

Criteria Number	Exclusion Criteria
26.	The Subject meets one or more of the following sleep study criteria as assessed by the Baseline PSG: a. An AHI < 15 or ≥ 65 b. Apnea Index (AI) >30 events per hour c. >25% mixed or central apnea events as a proportion of the sum of apnea and hypopnea events per hour d. Positional OSA as defined by non-supine AHI <5 when sufficient non supine sleep is available to make this judgement e. Predominantly rapid eye movement (REM) OSA (ratio between the AHI in REM and AHI in non-rapid eye movement (NREM) >2) f. Indication of a sleep disorder or poor sleep hygiene that could confound functional assessments of sleepiness such as poor sleep efficiency in the opinion of the investigator.

iii. Follow-Up Schedule

All subjects in the OSPREY Study were scheduled for follow-up examinations. Data collection at specified time points was based on evaluating safety and effectiveness. After successful screening and collection of baseline data including PSG tests, subjects were implanted with the aura6000™ system. Thereafter, between Day 7 and Day 20 subjects were randomized to treatment group. In parallel with the M1 in-office visit, therapy initiation (device activation) commenced during the required PSG test for the Treatment group only. Regular follow-up in-office visits occurred at 2, 3, 4, 5, 6, 7, 9, 11, and 13 months for the Treatment group. Additional PSG studies were required at 3, 6, and 7 months and as needed at 2, 4, and 5 months for the Treatment group. The Control group had regular follow-up in-office visits at 3, 5 and 7 months, and regularly scheduled phone calls at 2, 4, and 6 months during the RCT phase. Following the M7+1 day visit, the Control group had therapy initiated and followed the same initial schedule as the Active group. Primary evaluation of safety and effectiveness results occurred at M7 visit. The following schedule of events is provided as a summary of activities and time points in the OSPREY Study through M13 (**Table 18)**

Table 18. OSPREY Study Follow-Up Schedule

	All Groups				Active Group													
	Screening through Implant			Randomization	Randomization (RCT) Phase - Primary Treatment Comparison								Post-Randomization Phase - All Groups Treatment					
Time and Effort	Screening Visit(s)	Baseline	Implant	Randomize	Month 1 Active	Month 2 Active	Month 3 Active	Month 3+1D Active	Month 4 Active	Month 5 Active	Month 6 Active	Month 7 Active Primary Endpoint	Month 8 Active	Month 9 Active	Month 10 Active	Month 11 Active	Month 12 Active	Month 13 Active Exit PSG
Visit Number	1	2	3	4	5	6	7	7	8	9	10	11	12	13	14	15	16	17
Target Follow-up Post Implant / Window	^Up to 90 days prior to Consent	Up to Implant date	Day 0	Day 7 - 20	D 21-45	D 46-75	D 76-105	1 D following M3	D 106-135	D 136-165	D 166-195	D 196-225	D 226-255	D 256-285	D 286-315	D 316-345	D 346-375	D 376-405
Informed Consent/HIPAA	x																	
Inclusion/ Exclusion Criteria Review	x		x															
Subject Demographics & Medical History	x																	
Surgical Consultation	x																	
Upper Airway Exam	x																	
HGN/Tongue Function Assessment	x				x	x	x		x	x	x	x		x		x		x
Physical Exam (neck circum./healthy lifesty review)	x			x	x	x	x		x	x	x	x		x		x		x
Vital Signs (HT/WT/HR/BP)	x	x		x	x	x	x		x	x	x	x		x		x		x
Home Sleep Tests (2 HSTs up to a 3 night-time period)	x																	
PSG #1 (baseline to be done after HSTs)		x			x	x*	x		x*	x*	x	x	x*	x*	x*	x	x*	x
PSG #2								x										
Urine Pregnancy Test	x*		x*															
Implant Surgery			x															
Wound Check				x														
Randomization in EDC				x														
ESS		x										x						x
FOSQ		x										x						x
EQ-5D-5L		x										x						x
SF36		x										x						x
Clinical Global Impression S (CGI S)		x																
Clinical GlobalImpression I (CGI I)												x						x
PROMIS SRI SDI		x										x						x
Therapy Satisfaction Questionnaire												x						x
Therapy Initiation					x													
Subject Training					x	x*	x*	x*	x*	x*	x*	x*	x*	x*	x*	x*	x*	x*
Device Interrogation / sensory testing / Usage log download					X	x	x		x	x	x	x	x*	x	x*	x	x*	x
Phone Call													x		x		x	
Medication Review	x		x	x	x	x	x		x	x	x	x	x	x	x	x	x	x
Adverse event Review	x		x	x	x	x	x		x	x	x	x	x	x	x	x	x	x
Overall Subject Satisfaction Questionnaire																		x
Study Completion/Termination/Exit																		x
x = only if indicated*																		
^consent MUST occur before any solely study related activities																		

	All Groups				Control Group														
	Screening through Implant			Randomization	Randomization (RCT) Phase - Primary Treatment Comparison							Post-Randomization Phase - All Groups Treatment							
Time and Effort	Screening Visit(s)	Baseline	Implant	Randomize	Month 1 Control	Month 2 Control	Month 3 Control	Month 4 Control	Month 5 Control	Month 6 Control	Month 7 Control Primary Endpoint	Month 7+1D Control	Month 8 Control	Month 9 Control	Month 9+1D Control	Month 10 Control	Month 11 Control	Month 12 Control	Month 13 Control Exit PSG
Visit Number	1	2	3	4	5	6	7	8	9	10	11	11	12	13	13	14	15	16	17
Target Follow-up Post Implant / Window	^Up to 90 days prior to Consent	Up to Implant date	Day 0	Day 7 - 20	D 21-45	D 46-75	D 76-105	D 106-135	D 136-165	D 166-195	D 196-225	1 D following M7	D 226-255	D 256-285	1 D following M9	D 286-315	D 316-345	D 346-375	D 376-405
Informed Consent/HIPAA	x																		
Inclusion/ Exclusion Criteria Review	x		x																
Subject Demographics & Medical History	x																		
Surgical Consultation	x																		
Upper Airway Exam	x																		
HGN/Tongue Function Assessment	x				x		x		x		x		x	x		x	x	x	x
Physical Exam (neck circum./healthy lifesty review)	x			x	x		x		x		x		x	x		x	x	x	x
Vital Signs (HT/WT/HR/BP)	x	x		x	x		x		x		x		x	x		x	x	x	x
Home Sleep Tests (2 HSTs up to a 3 night-time period)	x																		
PSG #1 (baseline to be done after HSTs)		X									x	x	x*	x		X*	X*	X	x
PSG #2															x				
Urine Pregnancy Test	x*		x*																
Implant Surgery			x																
Wound Check				x															
Randomization in EDC				x															
ESS		x									x								x
FOSQ		x									x								x
EQ-5D-5L		x									x								x
SF36		x									x								x
Clinical Global Impression S (CGI S)		x																	
Clinical GlobalImpression I (CGI I)											x								x
PROMIS SRI SDI		x									x								x
Therapy Satisfaction Questionnaire																			x
Therapy Initiation												x	x	x		x	x	x	x
Subject Training												x	x*	x*	x*	x*	x*	x*	x*
Device Interrogation / sensory testing / Usage log download												x	x	x		x	x	x	x
Phone Call						x		x		x									
Medication Review	x		x	x	x	x	x	x	x	x	x		x	x		x	x	x	x
Adverse event Review	x		x	x	x	x	x	x	x	x	x		x	x		x	x	x	x
Overall Subject Satisfaction Questionnaire																			x
Study Completion/Termination/Exit																			x
x = only if indicated*																			
^consent MUST occur before any solely study related activities																			

iv. Clinical Endpoints

The primary objective of the study was to demonstrate the safety and effectiveness of the aura6000™ system after 6 months of stimulation therapy (Treatment Group) when compared to a control group with no stimulation, when used in patients with moderate to severe OSA.

a) Primary Safety Endpoints

The primary safety endpoint consisted of a descriptive evaluation of all reported serious adverse device effects (device-related SAEs; SADEs)[1] through M7 for both treatment arms (Treatment and Control Groups). The relationship of SADEs to the procedure, the device and the study were adjudicated by the Clinical Events Committee (CEC) and reviewed by the Data Safety Monitoring Board (DSMB).

b) Primary Effectiveness Endpoints

The primary effectiveness endpoint was to demonstrate that the AHI responder rate – defined as the percentage of subjects who show at least a 50% decrease in AHI from baseline to M7 and a M7 AHI value < 20 events/hr – was statistically significantly higher in the Treatment Group compared to the Control Group at M7.

c) Secondary Safety Endpoint

Descriptive evaluation of all adverse device events (ADEs)

d) Secondary Effectiveness Endpoints

The secondary effectiveness endpoints for this study were tested in the following fixed-sequence (hierarchical) order:

- Decrease in Oxygen Desaturation Index (ODI) of 50% between baseline and M7
- Change in Epworth Sleepiness Scale (ESS) between baseline and M7
- Change in Functional Outcomes of Sleep Questionnaire (FOSQ) between baseline and M7
- Change in Patient-Reported Outcomes Measurement Information System-Sleep Disturbance Index (PROMIS SDI) and Sleep Related Impairment (PROMIS SRI) between baseline and M7
- Change in Medical Outcomes Study 36-Item Health Survey Short Form (SF-36) between baseline and M7
- Change in EQ-5D-5L (Quality of Life Questionnaire) between baseline and M7.
- Change in Percentage of Total Sleep Time with Oxygen Saturation below 90% (T90) between baseline and M7

Clinical Global Impression-Improvement (CGI-I) at M7 was also tested outside the hierarchical sequence.

[1] **SADE:** Serious Adverse Device Effect. An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event (SAE). In other words, a SADE is a subset of SAEs, distinguished by device relatedness. **SAE**: Serious Adverse Event. An adverse event, regardless of causality, that results in one or more of following outcomes: death, serious deterioration of health, or fetal distress/death/birth defect. In other words, a SAE is defined strictly by severity and outcome, not relationship to the device or procedure.

v. Statistical Analysis

The primary efficacy endpoint is the AHI responder rate of subjects at 6 months after the device initiation (i.e., M7 visit). A responder in AHI was defined as a decrease in AHI of at least 50% between the baseline and M7 PSGs, and an AHI absolute value below 20 at the M7 PSG.

The primary analysis was based on all available data in the ITT Analysis Set.

The goal of the study was to demonstrate that the AHI responder rate of subjects with the device stimulation activated (Treatment) was statistically significantly higher than the AHI responder rate of subjects with the device not activated (Control) at M7.

The primary statistical hypothesis is:

- $\mathbf{H_0: P_{Stimulation} \leq P_{Control}}$
- $\mathbf{H_a: P_{Stimulation} > P_{Control}}$

where $P_{Stimulation}$ and $P_{Control}$ represent the AHI responder rate at M7 in the Active/Stimulation and Control groups respectively.

The primary efficacy analysis was conducted using Fisher's exact test comparing the AHI responder rates between the Treatment group and the Control group at M7. This trial was considered successful if the one-sided p-value comparing the two groups is less than or equal to 0.025. The study was planned to have 90% power with a mean sample size of approximately 122 evaluable subjects based on assumptions coming from the THN3 RCT conducted under IDE G140158. When all enrolled and randomized subjects were followed up at M7, the primary efficacy endpoint was analyzed in the ITT Population. Subjects missing response assessments, regardless of treatment status, were treated as non-response.

The timing and sample size of the final primary efficacy analysis was based on Bayesian inference with a Goldilocks design, with pre-defined early enrollment stop thresholds, conducted on the ITT Population at pre-defined interim analyses. Screening and consenting were completed and sites were notified that the enrollment phase was completed based on the interim analysis of 90 subjects and the determination that the 90 subjects who had been randomized had a predictive success rate of at least 97.5%. At the time of communication to the sites to halt further enrollment, any subject who had qualified and had an implant scheduled was permitted to move forward.

Three independent committees govern the study and conduct. A Steering Committee (SC) was appointed for general study development and oversight. A DSMB and CEC were appointed for safety oversight. An independent core lab scored all the sleep studies in order to minimize assessment bias.

vi. Accountability of PMA Cohort

Approximately 9,100 patients were prescreened at the start of the study. A total of 1,022 subjects consented to participate in the study. Of these, 905 subjects were subsequently screen-failed, with the most common reason being that their baseline PSG results did not meet protocol-specified inclusion criteria.

Among the 117 subjects that passed screening criteria, 10 did not proceed with implantation. Reasons for not being implanted included withdrawal of consent (n=3), an adverse event (n=1), physician decision (n=1), early study termination by the sponsor (n=1), unsuccessfully implanted (n=1), and achievement of the sponsor's enrollment targets (n=3). A total of 107 subjects were successfully implanted and subsequently randomized, with 69 assigned to the Treatment group and 38 to the Control group (**Figure 7**).

The analysis population included 104 of the 107 randomized subjects. Three subjects were excluded from the ITT analysis set in accordance with FDA guidance as they did not meet all inclusion and exclusion criteria.

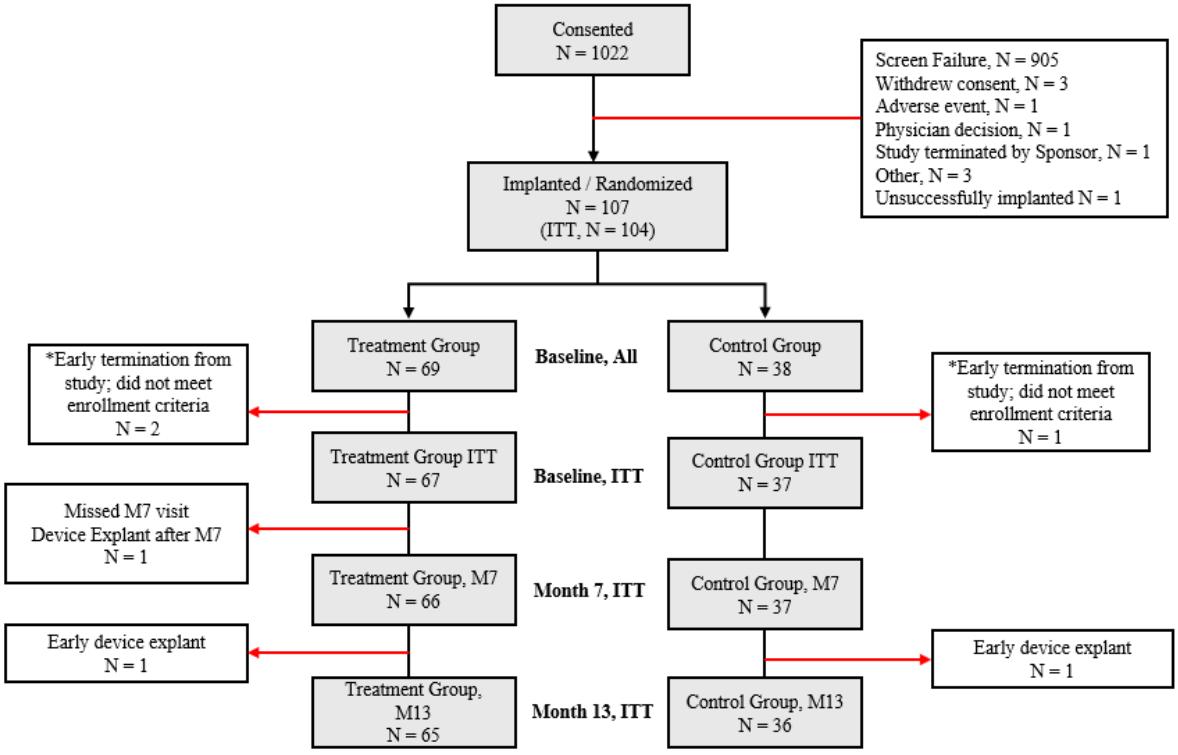

Figure 7. Consort Diagram of Subject Flow through the OSPREY Study

vii. Study Population Demographics and Baseline Parameters

Demographics and baseline characteristics are summarized by treatment group for the ITT Population in **Table 19,** and were evenly distributed among the groups. The population enrolled in OSPREY was typical of HGNS trials, consisting of overweight to obese individuals (mean BMI 30.6 kg/m^2), on average in the sixth decade of life (median age 56 years), who were predominantly male (73.1%) and white (87.5%) with a variety of comorbidities. Baseline OSA severity was similar between the treatment groups, with approximately 40% with moderate OSA ($15 \leq AHI \leq 30$) and approximately 60% with severe OSA ($AHI > 30$).

Table 19. Baseline Demographics and Clinical Characteristics for OSPREY Study

	Treatment (N = 67)	Control (N = 37)	Total (N = 104)
DEMOGRAPHIC CHARACTERISTICS			
Sex			
Female	18 (26.9%)	10 (27.0%)	28 (26.9%)
Male	49 (73.1%)	27 (73.0%)	76 (73.1%)
Age (years)			
Mean (SD)	55.8 (9.07)	55.1 (9.07)	55.6 (9.03)
Median	57.0	53.0	56.0
< 65 years	54 (80.6%)	31 (83.8%)	85 (81.7%)
≥ 65 years	13 (19.4%)	6 (16.2%)	19 (18.3%)
Ethnicity			
Hispanic or Latino	10 (14.9%)	8 (21.6%)	18 (17.3%)
Not Hispanic or Latino	56 (83.6%)	29 (78.4%)	85 (81.7%)
Not Reported	1 (1.5%)	0 (0%)	1 (1.0%)
Race			
White	58 (86.6%)	33 (89.2%)	91 (87.5%)
Black or African American	5 (7.5%)	1 (2.7%)	6 (5.8%)
American Indian or Alaska Native	1 (1.5%)	0 (0%)	1 (1.0%)
Asian	2 (3.0%)	1 (2.7%)	3 (2.9%)
Native Hawaiian or Other Pacific Islander	0 (0%)	0 (0%)	0 (0%)
Other	0 (0%)	1 (2.7%)	1 (1.0%)
Not Reported	1 (1.5%)	1 (2.7%)	2 (1.9%)
CLINICAL CHARACTERISTICS			
Baseline OSA Severity defined by AHI			
N	67	37	104
Mean (SD)	35.47 (13.278)	36.11 (11.976)	35.70 (12.275)
95% CI for the Mean	(32.23, 38.71)	(32.12, 40.10)	(33.21, 38.18)
Moderate, 15 ≤ AHI ≤ 30	27 (40.3%)	14 (37.8%)	41 (39.4%)
Severe, AHI > 30	40 (59.7%)	23 (62.2%)	63 (60.6%)
Body Mass Index (BMI)			
N	67	37	104
Mean (SD)	30.06 (3.007)	31.47 (2.787)	30.56 (2.995)
95% CI for the Mean	(29.32, 30.79)	(30.54, 32.40)	(29.98, 31.14)
< 32	44 (65.7%)	21 (56.8%)	65 (62.5%)
≥ 32	23 (34.3%)	16 (43.2%)	39 (37.5%)
Tonsil Grading Scale			
0	26 (38.8%)	14 (37.8%)	40 (38.5%)
1	30 (44.8%)	13 (35.1%)	43 (41.3%)
2	10 (14.9%)	10 (27.0%)	20 (19.2%)
Missing	1 (1.5%)	0 (0%)	1 (1.0%)

	Treatment (N = 67)	Control (N = 37)	Total (N = 104)
Lingual Tonsil Hypertrophy			
0	27 (40.3%)	8 (21.6%)	35 (33.7%)
1	29 (43.3%)	19 (51.4%)	48 (46.2%)
2	10 (14.9%)	10 (27.0%)	20 (19.2%)
Missing	1 (1.5%)	0 (0%)	1 (1.0%)
Neck Circumference (cm)			
N	67	37	104
Mean (SD)	41.25 (3.86)	41.88 (4.33)	41.47 (4.02)
95% CI for the Mean	(40.31, 42.19)	(40.44, 43.32)	(40.69; 42.26)
Time since initial OSA diagnosis from screening (years)			
N	67	37	104
Mean (SD)	7.7 (6.83)	7.6 (6.03)	7.6 (6.53)
95% CI for the Mean	(6.0, 9.3)	(5.6, 9.6)	(6.4; 8.9)
AHI from most recent PSG prior to study enrollment			
N	62	33	95
Mean (SD)	37.10 (17.130)	39.75 (20.365)	38.02 (18.255)
95% CI for the Mean	(32.74, 41.45)	(32.53, 46.97)	(34.30, 41.74)
ALTERNATIVE OSA TREATMENT HISTORY			
Former CPAP use	43 (64.2%)	26 (70.3%)	69 (66.3%)
Ongoing CPAP use	10 (14.9%)	4 (10.8%)	14 (13.5%)
Former BIPAP use	4 (6.0%)	3 (8.1%)	7 (6.7%)
Ongoing BIPAP use	1 (1.5%)	0 (0%)	1 (1.0%)
Former oral appliance use (all)	18 (26.9%)	7 (18.9%)	25 (24.0%)
Ongoing oral appliance use (all)	2 (3.0%)	3 (8.1%)	5 (4.8%)
Former Positional Device Use (all)	4 (6.0%)	0 (0%)	4 (3.8%)
Ongoing Positional Device Use (all)	3 (4.5%)	2 (5.4%)	5 (4.8%)
Number of Subjects who had Upper Airway Surgery	12 (17.9%)	6 (16.2%)	18 (17.3%)
Genioglossus advancement	1 (1.5%)	0 (0%)	1 (1.0%)
Uvulopalatopharyngoplasty (UPPP)	6 (9.0%)	2 (5.4%)	8 (7.7%)
Other[1] / Not listed	10 (14.9%)	5 (13.5%)	15 (14.4%)

[1] Other surgery included:
Treatment group: 8 tonsillectomy/adenoidectomy and 2 septoplasty
Control group: Septoplasty, tonsillectomy and left-sided maxillary sinus surgery

Abbreviations: AHI = Apnea hypopnea index; BiPAP = Bilevel positive airway pressure; CI = Confidence Interval; CPAP = Continuous positive airway pressure; OSA = Obstructive sleep apnea; PSG = Polysomnography; UPPP = Uvulopalatopharyngoplasty

The median skin-to-skin implant time in the OSPREY trial was 72.0 minutes (Mean 81.3 minutes, SD 31.8), with procedures ranging from 37 to 218 minutes. All implants were performed on an outpatient basis with same-day discharge.

viii. Safety and Effectiveness Results

a) Primary Safety Endpoint – Serious Adverse Device Effects (SADEs) – up to Month 7 (RCT)

No Unanticipated Adverse Device Effects (UADEs) or deaths were reported in either group. Four subjects had device-related surgical interventions that were reclassified as SADEs; however, neither the Study Investigator nor the Clinical Events Committee (CEC) originally classified these as SADEs based on the pre-specified SADE definition in the study protocol.

b) Secondary Safety Endpoint – Adverse Device Events

Adjudicated Treatment Emergent Adverse Events (TEAEs)

TEAEs – Up to Month 7 (RCT)

During the trial, a total of 261 TEAEs were reported in 81 subjects up to Month 7. In the Treatment group, 184 (70.5%) were reported in 57 subjects (85.1%) and in the Control group, 77 (29.5%) were reported in 24 subjects (64.9%) (**Table 20**). No UADEs or deaths were reported in either group. 4 surgical interventions were reported in 4 subjects, which were reclassified as SADEs. The majority (78.9%) of TEAEs were mild, and overall event rates were comparable between the Treatment and Control groups. All adverse events observed in the OSPREY study through M7 are summarized in **Table 20**.

TEAEs that occurred on the day of implant up to 30 days post-implant resulted in 118 TEAEs, with 36 subjects (53.7%) in the Treatment group (73 events) and 18 subjects (48.6%) in the Control group (45 events) reporting at least one (1) event. The TEAE severity profile was very similar through M7 in both treatment groups, and nearly half (118 events, 45.2%) occurred in the first 30 days after implant. For the Treatment group, 90.6% (163/180) of TEAEs with resolution information resolved/recovered with a mean (SD) duration of 50.5 (92.6) days and median of 16 days from onset. The Control group had 92.2% (71/77) resolved/recovered with a mean (SD) duration of 70.7 (85.8) days and median of 49 days from onset. Twenty-three (23) TEAEs (8.9%) were unresolved or ongoing at the time of data cutoff.

Among the 143 TEAEs reported once stimulation therapy was activated (i.e. 31 days after implantation; M1 visit) through Month 7, the most common events were COVID-19 (5.8% of subjects, 6 events) and hypertension (5.8% of subjects, 6 events) at the time of reporting.

Across both the treatment and control groups, 79.0% (113/143) of TEAEs after stimulation activation through Month 7 were classified as “mild”, 14.7% (21/143) as “moderate”, and 4.9% (7/143) as “severe”.

Implant procedure–related TEAEs were reported in 44.8% of subjects in the Treatment group and 35.1% in the Control group. As expected, most of these events occurred within 30 days

post-implant; 83% (50/60) in the Treatment group and 97% (34/35) in the Control group. The leading complaints related to procedure were implant site pain, dysphagia, headache, oropharyngeal pain, implant site swelling, tongue movement disturbance, and neck pain and are expected with this type of surgical procedure. Study-related TEAEs were similarly balanced, occurring in 56.7% of Treatment subjects and 45.9% of Control subjects. Among procedure-related TEAEs in the Treatment group, the mean (SD) duration to resolution/recovery was 44.2 (62.0) days with a median of 25 days from onset. For the Control group, the mean (SD) was 55.8 (53.0) days, and the median was 38 days.

Stimulation-related TEAEs were reported in 19% of subjects (13/67; 19 events) in the Treatment group and in no subjects in the Control group. The leading complaints related to stimulation were oropharyngeal sensory-motor symptoms in 10% of subjects describing symptoms such as glossodynia, tongue discomfort and dysphagia, and speech disorder. Device discomfort or pain were recorded in 9% of subjects. Among stimulation-related TEAEs in the Treatment group, the mean (SD) duration to resolution/recovery was 83.1 (172.0) days with a median of 22 days from onset.

Device-related TEAEs were infrequent, with 10 events reported in the Treatment group, most of which occurred more than 30 days post-implant, and one event reported in the Control group. All device-related TEAEs were resolved/recovered, with a mean (SD) duration of 17.1 (21.5) days and a median time of 4 days from onset.

From implant through M7, the most reported TEAE was headache (Treatment: 16.4% of subjects; 11 events; Control: 9.0% of subjects; 7 events). Other frequent TEAEs in the Treatment group included implant site pain (11.9% of subjects; 8 events), dysphagia (10.4% of subjects; 7 events), COVID-19 (9.0% of subjects; 6 events), ear pain (7.5% of subjects; 6 events), and neck pain (6.0% of subjects; 6 events). In the Control group, the most frequently reported TEAEs, aside from headache, included oropharyngeal pain (10.8% of subjects; 4 events), as well as ear pain, neck pain, glossodynia, and implant site pain (each reported in 5.4% of subjects; 3 events each). See **Table 21** for all TEAEs reported in at least 2% of subjects by AE term.

Table 20. Adjudicated Treatment Emergent Adverse Events up to 7 Months for OSPREY Study

	Treatment (N=67)			Control (N=37)			Total (N=104)		
	n (%)		e	n (%)		e	n (%)		e
Treatment Emergent Adverse Event (TEAE)	**57**	**(85.1%)**	**184**	**24**	**(64.9%)**	**77**	**81**	**(77.9%)**	**261**
Serious TEAE*	4	(6.0%)	4	2	(5.4%)	2	6	(5.8%)	6
Non-serious TEAE	57	(85.1%)	180	24	(64.9%)	75	81	(77.9%)	255
Mild TEAE	55	(82.1%)	146	23	(62.2%)	60	78	(75.0%)	206
Moderate TEAE	16	(23.9%)	30	8	(21.6%)	10	24	(23.1%)	40
Severe TEAE	2	(3.0%)	4	2	(5.4%)	7	4	(3.8%)	11
Study Related	**38**	**(56.7%)**	**107**	**17**	**(45.9%)**	**50**	**55**	**(52.9%)**	**157**
Occurring ≤ 30 days post implant	31	(46.3%)	61	15	(40.5%)	40	46	(44.2%)	101
Occurring ≥ 31 days post implant	24	(35.8%)	46	5	(13.5%)	10	29	(27.9%)	56
Related to the Implant Procedure	**30**	**(44.8%)**	**60**	**13**	**(35.1%)**	**35**	**43**	**(41.3%)**	**95**
Occurring ≤ 30 days post implant	27	(40.3%)	50	13	(35.1%)	34	40	(38.5%)	84
Occurring ≥ 31 days post implant	7	(10.4%)	10	1	(2.7%)	1	8	(7.7%)	11
Related to Stimulation	**13**	**(19.4%)**	**19**	**0**	**(0%)**	**0**	**13**	**(12.5%)**	**19**
Occurring ≤ 30 days post implant	1	(1.5%)	2	0	(0%)	0	1	(1.0%)	2
Occurring ≥ 31 days post implant	12	(17.9%)	17	0	(0%)	0	12	(11.5%)	17
Device Related	**9**	**(13.4%)**	**10**	**1**	**(2.7%)**	**1**	**10**	**(9.6%)**	**11**
Occurring ≤ 30 days post implant	3	(4.5%)	3	0	(0%)	0	3	(2.9%)	3
Occurring ≥ 31 days post implant	6	(9.0%)	7	1	(2.7%)	1	7	(6.7%)	8
TEAE leading to device explanted	**0**	**(0%)**	**0**	**2**	**(5.4%)**	**7**	**2**	**(1.9%)**	**7**
TEAE caused the subject to discontinue the study	**0**	**(0%)**	**0**	**1**	**(2.7%)**	**1**	**1**	**(1.0%)**	**1**
Deaths	0	(0%)	0	0	(0%)	0	0	(0%)	0
Unanticipated Adverse Device Effects (UADE)	0	(0%)	0	0	(0%)	0	0	(0%)	0
Serious Adverse Device Effect (SADE)	4	(6.0%)	4	0	(0%)	0	4	(3.8%)	4

n= number of subjects with at least one AE
%= percentage of subjects with at least one AE
e= number of AEs
*4 Surgical intervention events were not adjudicated by the Study Investigator or the Clinical Events Committee as serious adverse events (SAEs) or serious adverse device effects (SADEs). Excluding these events would result in 0 SADEs Overall, 0 SAEs in the Stimulation group, and 2 SAEs/SADEs across 2 Control subjects.

Table 21. Adjudicated TEAEs Occurring in ≥2% of Subjects Through Month 7

AE Term	Treatment (N=67) n (%)	Control (N=37) n (%)	Total (n=104) n (%)
Headache	11 (16.4%)	6 (16.2%)	17 (16.3%)
Implant site pain	8 (11.9%)	2 (5.4%)	10 (9.6%)
Oropharyngeal pain	4 (6.0%)	4 (10.8%)	8 (7.7%)
Ear pain	5 (7.5%)	2 (5.4%)	7 (6.7%)
Dysphagia	7 (10.4%)	0 (0%)	7 (6.7%)
COVID-19	6 (9.0%)	1 (2.7%)	7 (6.7%)
Glossodynia	4 (6.0%)	2 (5.4%)	6 (5.8%)
Neck pain	4 (6.0%)	2 (5.4%)	6 (5.8%)
Hypertension	4 (6.0%)	2 (5.4%)	6 (5.8%)
Nasopharyngitis	3 (4.5%)	2 (5.4%)	5 (4.8%)
Upper respiratory tract infection	4 (6.0%)	1 (2.7%)	5 (4.8%)
Implant site swelling	3 (4.5%)	1 (2.7%)	4 (3.8%)
Fall	3 (4.5%)	1 (2.7%)	4 (3.8%)
Tongue movement disturbance	4 (6.0%)	0 (0%)	4 (3.8%)
Tinnitus	2 (3.0%)	1 (2.7%)	3 (2.9%)
Odynophagia	1 (1.5%)	2 (5.4%)	3 (2.9%)
Medical device discomfort	3 (4.5%)	0 (0%)	3 (2.9%)
Sinusitis	2 (3.0%)	1 (2.7%)	3 (2.9%)
Musculoskeletal discomfort	3 (4.5%)	0 (0%)	3 (2.9%)
Dysarthria	2 (3.0%)	1 (2.7%)	3 (2.9%)
Hypoaesthesia	2 (3.0%)	1 (2.7%)	3 (2.9%)
Hypoaesthesia oral	2 (3.0%)	1 (2.7%)	3 (2.9%)
Speech disorder	3 (4.5%)	0 (0%)	3 (2.9%)
Cough	2 (3.0%)	1 (2.7%)	3 (2.9%)
n= number of subjects reporting the AE %= percentage of subjects reporting the AE			

TEAEs – Month 7 to Month 13

Between Month 7 and Month 13, an additional 136 TEAEs were reported. The TEAE severity profile was consistent with the randomization phase of the study. In the Crossover phase (M7+1D to M13), 98of the 136 TEAEs (72.1%) were classified as mild. The most common (> 5% of subjects reporting) of the 136 TEAEs reported in this timeframe was

Nasopharyngitis (5.8% of subjects, 6 events) with no other events being seen in > 5% of subjects.

TEAEs – Up to Month 13

From implant through M13, the most commonly reported TEAE was headache (18.3% of subjects, 21 events), implant site pain (9.6% subjects, 11 events), oropharyngeal pain (8.7% of subjects, 9 events), ear pain (7.7% of subjects, 10 events), dysphagia (7.7% of subjects, 8 events), COVID-19 (10.6% of subjects, 11 events), hypertension (9.6% of subjects, 10 events), neck pain (7.7% of subjects, 12 events), and glossodynia (6.7% of subjects, 8 events).

An overview of all TEAEs through Month 13 is shown in **Table 22**, with additional detail depicted in **Table 23**. Throughout the study, 304 of the 397 TEAEs (76.6%) were mild. Only 21.2% of the subjects reported any stimulation-related adverse events.

Table 22. **Summary of Adjudicated TEAEs Through Month 13**

Adverse Events	**Non-device-related and Non-procedure-related Events e (n, %)**	**Device-related or Procedure-related Events e (n, %)**
Non-serious	289 (88, 84.6%)	106 (47, 45.2%)
Serious	6 (5, 4.8%)	14 (11, 10.6%)*

n: number of subjects with at least one event
% = (n/T X 100, where T is the total number of subjects in the ITT population)
e = number of events
Note: A subject can have more than one event
* The 14 serious adverse device effects (SADEs) include 4 explants, 5 IPG interventions, 4 lead replacement/IPG interventions, and 1 lead repositioning/IPG intervention that were not originally adjudicated by the Study Investigator or the Clinical Events Committee as serious adverse events (SAEs) or serious adverse device effects (SADEs). Excluding these events would result in 6 SAEs, none of which were device or procedure related.

Table 23. Adjudicated Treatment Emergent Adverse Events up to 13 Months for OSPREY Study

	Stimulation (N=67) n (%)	e	Control (N=37) n (%)	e	Total (N=104) n (%)	e
Treatment Emergent Adverse Event (TEAE)	**63 (94.0%)**	**275**	**30 (81.1%)**	**122**	**93 (89.4%)**	**397**
Serious TEAE*	10 (14.9%)	13	5 (13.5%)	7	15 (14.4%)	20
Non-serious TEAE	63 (94.0%)	262	29 (78.4%)	115	92 (88.5%)	377
Mild TEAE	62 (92.5%)	210	27 (73.0%)	94	89 (85.6%)	304
Moderate TEAE	25 (37.3%)	48	12 (32.4%)	17	37 (35.6%)	65
Severe TEAE	4 (6.0%)	7	2 (5.4%)	7	6 (5.8%)	14
Study Related	43 (64.2%)	117	18 (48.6%)	62	61 (58.7%)	179
Related to the Implant Procedure	31 (46.3%)	61	13 (35.1%)	36	44 (42.3%)	97
Related to Stimulation	17 (25.4%)	26	5 (13.5%)	7	22 (21.2%)	33
Device Related	13 (19.4%)	18	3 (8.1%)	5	16 (15.4%)	23
Related Other	5 (7.5%)	5	4 (10.8%)	10	9 (8.7%)	15
TEAE leading to device explanted	1 (1.5%)	2	2 (5.4%)	7	3 (2.9%)	9
TEAE caused the subject to discontinue the study	0 (0%)	0	1 (2.7%)	1	1 (1.0%)	1
Deaths	0 (0%)	0	0 (0%)	0	0 (0%)	0
Serious Adverse Device Effect (SADE)*	8 (11.9%)	10	3 (8.1%)	4	11 (10.6%)	14

n= number of subjects with at least one AE
%= percentage of subjects with at least one AE
e= number of AEs
* 14 Surgical intervention events were not adjudicated by the Study Investigator or the Clinical Events Committee as serious adverse events (SAEs) or serious adverse device effects (SADEs). Excluding these events would result in 0 SADEs Overall, 3 SAEs across 2 Stimulation subjects, and 3 SAEs across 3 Control subjects.

The occurrence of all TEAEs by time since implant is shown in **Table 24**. In both groups, fewer events were reported later in the study during the crossover when the Control group began receiving stimulation.

Table 24. All Treatment Emergent Adverse Events up to 13 Months by study period

Original randomization	Months 0 – 7 RCT		Months 7 – 13 Control Crossover		Months 0 – 13	
	n (%)	events	n (%)	events	n (%)	events
Treatment (N=67)	57 (85.1%)	184	46 (68.7%)	91	63 (94.0%)	275
Control (N=37)	24 (64.9%)	77	22 (59.5%)	45	30 (81.1%)	122
All (N=104)	81 (77.9%)	261	68 (65.4%)	136	93 (89.4%)	397
n= number of subjects with at least one AE %= percentage of subjects with at least one AE						

The occurrence of stimulation-related adverse events by time since implant is summarized in **Table 25**. During the first six months of therapy, stimulation-related adverse events were reported by 19.4% and 13.5% of the Treatment and Control subjects, respectively. Among subjects in the Treatment group who received therapy during both study periods, the incidence of stimulation-related adverse events decreased over time, with only 6.0% of subjects reporting such events in Months 7 to 13, corresponding to the second six months of therapy.

Table 25. Stimulation-Related Adverse Events up to 13 Months by study period

Original randomization	Months 0 – 7 RCT		Months 7 – 13 Control Crossover		Months 0 – 13	
	n (%)	events	n (%)	events	n (%)	events
Treatment (N=67)	13 (19.4%)	19	4 (6.0%)	7	17 (25.4%)	26
Control (N=37)	0 (0%)	0	5 (13.5%)	7	5 (13.5%)	7
All (N=104)	13 (12.5%)	19	9 (8.7%)	14	22 (21.2%)	33
n= number of subjects with at least one AE %= percentage of subjects with at least one AE						

Serious Adverse Events (SAEs) and Serious Adverse Device Effects (SADEs)

SAEs – Up to Month 7 (RCT)

Two TEAEs were classified as SAEs by the Investigator and CEC, occurring in separate subjects from the Control group (5.4%, 2/37), and were not related to the study, implant procedure, stimulation, or device, and all were reported as resolved or recovered. While not meeting the pre-specified definition of SADEs in the study protocol, an additional 4 events of surgical intervention were reclassified as SADEs, resulting in a total SAE and SADE incidence of 5.8%, 3.8% device-related, through Month 7. See **Table 26**.

Table 26. Overview of Adjudicated Serious Adverse Events (including Serious Adverse Device Effects) up to 7 Months by System Organ Class for OSPREY Study

System Organ Class	Treatment (N=67)				Control (N=37)				Total (N=104)			
Preferred Term	**n**	**(%)**	**e**	**IR**	**n**	**(%)**	**e**	**IR**	**n**	**(%)**	**e**	**IR**
Overall	**4**	**(6.0%)**	**4**	**(9.8)**	**2**	**(5.4%)**	**2**	**(9.3)**	**6**	**(5.8%)**	**6**	**(9.6)**
Cardiac disorders	**0**	**(0%)**	**0**	**(0)**	**1**	**(2.7%)**	**1**	**(4.7)**	**1**	**(1.0%)**	**1**	**(1.6)**
Pericarditis	0	(0%)	0	(0)	1	(2.7%)	1	(4.7)	1	(1.0%)	1	(1.6)
Gastrointestinal disorders	**0**	**(0%)**	**0**	**(0)**	**1**	**(2.7%)**	**1**	**(4.7)**	**1**	**(1.0%)**	**1**	**(1.6)**
Umbilical hernia	0	(0%)	0	(0)	1	(2.7%)	1	(4.7)	1	(1.0%)	1	(1.6)
Surgical intervention*	**4**	**(6.0%)**	**4**	**(9.8)**	**0**	**(0%)**	**0**	**(0)**	**4**	**(3.8%)**	**4**	**(6.4)**
IPG revision	1	(1.5%)	1	(2.5)	0	(0%)	0	(0)	1	(1.0%)	1	(1.6)
Lead Replacement/ IPG Revision	2	(3.0%)	2	(4.9)	0	(0%)	0	(0)	2	(1.9%)	2	(3.2)
Lead Repositioning/ IPG Revision	1	(1.5%)	1	(2.5)	0	(0%)	0	(0)	1	(1.0%)	1	(1.6)

n= number of subjects with at least one AE
%= percentage of subjects with at least one AE
e= number of AEs
IR= AE incidence rate per 100 patient-years of exposure = 100* (Number of events / Sum of PY)
Subjects may be counted in more than one SOC and in more than one PT
*4 Surgical intervention events were not adjudicated by the Study Investigator or the Clinical Events Committee as serious adverse events (SAEs) or serious adverse device effects (SADEs). Excluding these events would result in 0 SAEs in the Stimulation group, and 2 SAEs across 2 Control subjects.

Details of the four surgical interventions for device revision performed in four Treatment group subjects (4%) are presented in **Table 27**.

Table 27. aura6000™ Explants and Reinterventions in Treatment Group, up to 7 Months Post-Implant for OSPREY Study

Subjects	Days from implant	Original randomization	Revision type	Reason for revision
Subject 1	168	Treatment	Lead replacement	Not feeling stimulation
			Pocket revision	Not feeling stimulation
Subject 2	70	Treatment	Lead replacement	Unrelated AE-Fall/blunt trauma
			IPG replacement	Subject Request
Subject 3	84	Treatment	Pocket revision	Insufficient charging
Subject 4	63	Treatment	Lead repositioned	Not feeling stimulation

SAEs and SADEs – Month 7 to Month 13

Four TEAEs were classified as SAEs in the period from 7 to 13 months: three events in two Treatment subjects and one event in one Control subject, and were not related to the study, implant procedure, stimulation, or device, and all were reported as resolved or recovered. While not meeting the pre-specified definition of SADEs in the study protocol, an additional 10 events of surgical intervention in 8 subjects were reclassified as SADEs, resulting in a total SAE and SADE incidence of 10.6%, 7.7% device related, from Month 7 to Month 13. See **Table 28**.

Table 28. Overview of Adjudicated Serious Adverse Events from 7 to 13 Months by System Organ Class for OSPREY Study

System Organ Class Preferred Term	Stimulation N=67 (PY=35.5)				Control N=37 (PY=20.5)				TOTAL N=104 (PY=56)			
	n	(%)	e	(IR)	n	(%)	e	(IR)	n	(%)	e	(IR)
Overall*	**7**	**(10.4%)**	**9**	**(25.4)**	**4**	**(10.8%)**	**5**	**(24.4)**	**11**	**(10.6%)**	**14**	**(25.0)**
Gastrointestinal disorders	**1**	**(1.5%)**	**2**	**(5.6)**	**0**	**(0%)**	**0**	**(0)**	**1**	**(1.0%)**	**2**	**(3.6)**
Diverticulitis	1	(1.5%)	1	(2.8)	0	(0%)	0	(0)	1	(1.0%)	1	(1.8)
Large intestine perforation	1	(1.5%)	1	(2.8)	0	(0%)	0	(0)	1	(1.0%)	1	(1.8)
Hepatobiliary disorders	**1**	**(1.5%)**	**1**	**(2.8)**	**0**	**(0%)**	**0**	**(0)**	**1**	**(1.0%)**	**1**	**(1.8)**
Cholelithiasis	1	(1.5%)	1	(2.8)	0	(0%)	0	(0)	1	(1.0%)	1	(1.8)
Infections and infestations	**0**	**(0%)**	**0**	**(0)**	**1**	**(2.7%)**	**1**	**(4.9)**	**1**	**(1.0%)**	**1**	**(1.8)**
Pneumonia	0	(0%)	0	(0)	1	(2.7%)	1	(4.9)	1	(1.0%)	1	(1.8)
Surgical Re-intervention*	**5**	**(7.5%)**	**6**	**(16.9)**	**3**	**(8.1%)**	**4**	**(19.5)**	**8**	**(7.7%)**	**10**	**(17.9)**
Explant	2	(3.0%)	2	(5.6)	2	(5.4%)	2	(9.8)	4	(3.8%)	4	(7.1)
IPG Re-intervention	3	(4.5%)	3	(8.5)	1	(2.7%)	1	(4.9)	4	(3.8%)	4	(7.1)
Lead Replacement/IPG Re-intervention	1	(1.5%)	1	(2.8)	1	(2.7%)	1	(4.9)	2	(1.9%)	2	(3.6)

n= number of subjects with at least one AE
%= percentage of subjects with at least one AE
e= number of AEs
IR= AE incidence rate per 100 patient-years of exposure = 100* (Number of events / Sum of PY)
Subjects may be counted in more than one SOC and in more than one PT
*10 Surgical Re-intervention events were not adjudicated by the Study Investigator or the Clinical Events Committee as serious adverse events (SAEs) or serious adverse device effects (SADEs). Excluding these events would result in 3 SAEs across 2 Stimulation subjects, and 1 SAE in 1 Control subject.

Table 29 presents detail on the ten interventions among eight subjects performed from Month 7 through Month 13. One of these subjects had an unrelated intervention during the

initial M7 period. According to the original randomization, five of the subjects were from the Treatment group and three from the Control group. Two subjects from each group had the entire system explanted, although one of them later received a reimplant to continue the study.

Table 29. aura6000™ Explants and Reinterventions in Treatment Group, 7 to 13 Months Post-Implant for OSPREY Study

Subjects	Days from implant	Original randomization	Revision type	Reason for revision
Subject 3	326	Treatment	System explant	Device deficiency
Subject 5	224	Treatment	IPG replacement	Device deficiency
	355	Treatment	Lead replacement	Lead inadvertently pulled off nerve during prior revision surgery
Subject 6	363	Treatment	Pocket revision	Insufficient charging
Subject 7	366	Treatment	System explant	Subject choice due to underlying neuromuscular condition
Subject 8	326	Treatment	Pocket revision	Adverse event of pain on right side of neck
Subject 9	282	Control	Pocket revision	Insufficient charging
Subject 10	266	Control	System explant	Not feeling stimulation. During attempted revision surgery, system explanted due to excessive scarring.
Subject 11	291	Control	System explant	Adverse event of tightness in neck
	452	Control	IPG reimplant	Subject opted to be reimplanted and continue the study
			Lead reimplant	Subject opted to be reimplanted and continue the study

SAEs and SADEs – Up to Month 13

Six TEAEs, across five subjects, were classified as SAEs up to 13 months in accordance with the SAE definition pre-specified in the study protocol, none of which were related to the study, implant procedure, stimulation, or device, and all were reported as resolved or recovered. An additional 14 events of surgical intervention in 11 subjects were reclassified as SADEs, yielding a total incidence of device-related SAEs of 10.6% through Month 13. See **Table 30**.

Table 30. Overview of Serious Adverse Events and Serious Adverse Device Effects up to 13 Months by System Organ Class for OSPREY Study

System Organ Class Preferred Term	Stimulation (N=67) n (%)	e	IR	Control (N=37) n (%)	e	IR	Total (N=104) n (%)	e	IR
Overall	**10 (14.9%)**	**13**	**(17.0)**	**5 (13.5%)**	**7**	**(16.7)**	**15 (14.4%)**	**20**	**(16.9)**
Cardiac disorders	**0 (0%)**	**0**	**(0)**	**1 (2.7%)**	**1**	**(2.4)**	**1 (1.0%)**	**1**	**(0.8)**
Pericarditis	0 (0%)	0	(0)	1 (2.7%)	1	(2.4)	1 (1.0%)	1	(0.8)
Gastrointestinal disorders	**1 (1.5%)**	**2**	**(2.6)**	**1 (2.7%)**	**1**	**(2.4)**	**2 (1.9%)**	**3**	**(2.5)**
Diverticulitis	1 (1.5%)	1	(1.3)	0 (0%)	0	(0)	1 (1.0%)	1	(0.8)
Large intestine perforation	1 (1.5%)	1	(1.3)	0 (0%)	0	(0)	1 (1.0%)	1	(0.8)
Umbilical hernia	0 (0%)	0	(0)	1 (2.7%)	1	(2.4)	1 (1.0%)	1	(0.8)
Hepatobiliary disorders	**1 (1.5%)**	**1**	**(1.3)**	**0 (0%)**	**0**	**(0)**	**1 (1.0%)**	**1**	**(0.8)**
Cholelithiasis	1 (1.5%)	1	(1.3)	0 (0%)	0	(0)	1 (1.0%)	1	(0.8)
Infections and infestations	**0 (0%)**	**0**	**(0)**	**1 (2.7%)**	**1**	**(2.4)**	**1 (1.0%)**	**1**	**(0.8)**
Pneumonia	0 (0%)	0	(0)	1 (2.7%)	1	(2.4)	1 (1.0%)	1	(0.8)
Surgical intervention*	**8 (11.9%)**	**10**	**(13.1)**	**3 (8.1%)**	**4**	**(9.5)**	**11 (10.6%)**	**14**	**(11.8)**
Explant	2 (3.0%)	2	(2.6)	2 (5.4%)	2	(4.8)	4 (3.8%)	4	(3.4)
IPG Revision	4 (6.0%)	4	(5.2)	1 (2.7%)	1	(2.4)	5 (4.8%)	5	(4.2)
Lead Replacement/ IPG Revision	3 (4.5%)	3	(3.9)	1 (2.7%)	1	(2.4)	4 (3.8%)	4	(3.4)
Lead Repositioning/ IPG Revision	1 (1.5%)	1	(1.3)	0 (0%)	0	(0)	1 (1.0%)	1	(0.8)

n= number of subjects with at least one AE
%= percentage of subjects with at least one AE
e= number of AEs
IR= AE incidence rate per 100 patient-years of exposure = 100* (Number of events / Sum of PY)
Subjects may be counted in more than one SOC and in more than one PT
*14 Surgical intervention events were not adjudicated by the Study Investigator or the Clinical Events Committee as serious adverse events (SAEs) or serious adverse device effects (SADEs). Excluding these events would result in 3 SAEs across 2 Stimulation subjects, and 3 SAEs across 3 Control subjects.

Three subjects had two separate surgical interventions, including a reimplant surgery for a subject who chose to continue in the study following a system explant. All surgical interventions by type and by study period are shown in **Table 31**. Causes for the surgical interventions are reported in **Table 32**, with detailed event descriptions by subject in **Table 33**.

Table 31. Surgical intervention by type up to 13 Months by study period

Surgical intervention type in ITT (N=104)	Months 0 – 7 RCT		Months 7 – 13 Control Crossover		Months 0 – 13	
	n (%)	events	n (%)	events	n (%)	events
System explant	0 (0%)	0	4 (3.8%)	4	4 (3.8%)	4
IPG and Lead replacement	1 (1.0%)	1	1 (1.0%)	1	2 (1.9%)	2
IPG replacement	0 (0%)	0	1 (1.0%)	1	1 (1.0%)	1
Lead replacement	1 (1.0%)	1	1 (1.0%)	1	2 (1.9%)	2
Lead repositioning	1 (1.0%)	1	0 (0%)	0	1 (1.0%)	1
Pocket revision	1 (1.0%)	1	3 (2.9%)	3	4 (3.8%)	4
All types	4 (3.8%)	4	8 (7.7%)	10	11 (10.6%)	14
n= number of subjects with at least one event %= percentage of subjects with at least one event						

Table 32. Causes of Surgical Interventions

Reason	Events #	Description
Lead length	4	Throughout most of the OSPREY study conduct, only the shorter 25 cm lead option was available; eight implants of the 33 cm lead occurred late in the study and all other implants were the 25 cm lead. The shorter lead length may have been a contributing factor to four events: cuff dislodgement following a patient fall (Subject 2), cuff dislodgement following strenuous exercise (Subject 10), pocket revision due to pain on right side of neck due to tension on lead (Subject 8), and revision following adverse event of tightness in neck (Subject 11). The Physician's Manual was updated to provide guidance on selecting the proper lead length.
Implant depth	3	Charging the IPG was unsuccessful for three subjects (Subjects 3, 6, 9). A pocket revision to remove adipose tissue and decrease the depth of the implant resolved the issue in each case. The Physician's Manual was updated to clarify that insufficient implant depth may result in the patient not receiving therapy.
Loss of electrical isolation	2	A specific device malfunction of the IPG occurred in two subjects (Subjects 3, 5). Corrective actions were implemented to the design to prevent future occurrences.

Reason	Events #	Description
Cuff repositioning needed	2	Subject 4 had a lack of motor activation when the therapy was started. The cuff was not on the hypoglossal nerve, and this was resolved with a lead repositioning surgery. Subject 5 had the lead inadvertently pulled off the nerve during a prior revision surgery.
Wrong nerve	1	Subject 1 had the lead implanted on a structure that was not the hypoglossal nerve. The Physician's Manual provides instructions to test motor activation during the implant surgery to prevent this occurrence.
Neuromuscular condition	1	Subject 7 had an underlying congenital condition of nemaline myopathy that prevented them from tolerating the device, and they opted to have the system removed. Neuromuscular conditions were an exclusion criterion for OSPREY, but this condition was not reported at enrollment.
Re-implant	1	Subject 11 opted to be re-implanted. Previously they had attempted revision surgery to resolve a lead issue, and due to fibrosis, the revision took longer than expected resulting in a system explant.

Table 33. Description of All Surgical Interventions by Subject

Subject	Detailed Event Description
Subject 1 (Treatment)	Three months after implant, the subject reported lack of perception of stimulation. During revision surgery on Day 168 it was discovered that the lead was implanted on the wrong nerve. The lead was replaced and attached to the existing IPG to resolve the issue.
Subject 2 (Treatment)	The patient sustained an injury after a fall. Afterwards, X-rays revealed that the lead cuff had dislodged from the nerve. During the revision surgery on Day 70, the lead was replaced to resolve the issue, and the generator was replaced per patient request.
Subject 3 (Treatment)	The IPG was unable to connect to the charging antenna. The investigator determined the depth of the IPG was the root cause of not being able to connect and charge the IPG as the subject had a lot of adipose tissue around the IPG placement area. The investigator scheduled and performed a pocket revision on Day 84 to remove a layer of adipose tissue to decrease the pocket depth. The subject was then able to charge the IPG.
Subject 4 (Treatment)	At the M1 PSG, the subject was unable to feel the stimulation. The lead cuff was not on the hypoglossal nerve, and this was resolved with lead repositioning surgery on Day 63.
Subject 5 (Treatment)	A device deficiency was reported when the patient indicated that they could not feel the stimulation. The root cause was loss of electrical isolation on the IPG. The IPG was replaced on Day 224. The subject's system later reported high impedance. This was determined to be related to the surgeon inadvertently pulling the lead from the nerve during the IPG replacement. A lead replacement surgery on Day 355 resolved the issue.

Subject	Detailed Event Description
Subject 6 (Treatment)	The patient was unable to charge their device. A pocket revision on Day 363 to remove adipose tissue along with replacing the charging device resolved the issue.
Subject 7 (Treatment)	The subject had an underlying congenital condition of nemaline myopathy that prevented them from tolerating the device, and they opted to have the system removed on Day 366.
Subject 8 (Treatment)	The patient reported an adverse event of pain under the jaw due to tension on the lead. A pocket revision on Day 326 to adjust the position of the generator resolved the issue.
Subject 9 (Control)	The patient reported charging difficulties owing to an inconsistent magnetic alignment between the charging antennae and IPG. A pocket revision on Day 282 removed excess adipose tissue and resolved the charging difficulties.
Subject 10 (Control)	The subject did not perceive stimulation. The subject reported regular strenuous weight training. During an attempted revision surgery on Day 266, excessive scarring around the nerve site caused the surgery to end prematurely, and the system was explanted.
Subject 11 (Control)	The subject reported tightness in neck related to a lead pulling sensation. A revision surgery occurred on Day 291, but the lead revision was prolonged. The surgeon elected to explant the generator and lead. The subject later had a generator and lead re-implanted on Day 452.

Device Deficiencies

Device Deficiency (DD) was defined in the study protocol as any inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. These include malfunctions, use errors, and inadequate labeling. A total of 103 DDs (in 51 subjects) were reported up to M7 of the study.

Within the Treatment group, 43 subjects (64.2%) reported 95 DDs and 8 subjects (21.6%) in the Control group reported 8 DDs prior to M7. Overall, 101/103 (98.1%) of the DD's were resolved.

The severity of the device deficiencies was generally mild with 100 of the 103 (97.1%) not related to an AE or resolved with either no action taken or resolved with troubleshooting. The majority of DDs (94/103 (91.2%)) were not related to an adverse event. Of the 9 related to an AE, 6 were related to a Mild AE, 1 was related to a moderate severity AE, and 2 were related to a severe AE. The two severe adverse events included a fall in a subject which led to a lead dislodgement. The lead was successfully replaced. The second severe event was excessive scarring and fibrosis around the lead cuff in a subject which was found during an attempted revision surgery and led to a system explant. This subject eventually had their system re-implanted during the long-term follow-up portion of the study after M13.

Table 34 shows a breakdown of the 103 device deficiencies reported prior to M7 by device component and randomization group. Of the 103 total DDs reported, the most common components involved were the CA and RCC, each with 32 DDs (64 total (63%)). The Lead

and IPG accounted for 20 (19%) and 14 (14%), respectively. Of the 103 total DDs reported, 69 (68%) were reported in components that are not implanted (i.e., CA, aCM, RCC, RCC Power Cord).

Table 34. Device deficiency reports by component up to M7

Component	Treatment (N=67)	Control (N=37)	Total (N=104)
Charging Antenna (CA)	32	0	32
Clinical Manager Software (aCM)	2	1	3
IPG	14	0	14
Lead	13	7	20
Remote Control Charger (RCC)	32	0	32
RCC Power Cord	2	0	2
Total	**95**	**8**	**103**

A total of 56 additional DDs (in 41 subjects) were reported from M7 to M13 in the study.

Within the Treatment group, 25 subjects (37.3%) reported 31 DDs and 16 subjects (43.2%) in the Control group reported 25 DDs in this time period. Overall, 50/56 (89.3%) were resolved.

Table 35 shows a breakdown of the 56 device deficiencies reported from M7 to M13 by device component and original randomization group. Of the 56 DDs reported, the most common components involved were the CA (21) and RCC (17) or a combination/subset of these (3), with 41 total (73%). The Lead and IPG accounted for 5 (9%) and 9 (16%), respectively. Of the 56 DDs reported in this period, 42 (75%) were reported in components that are not implanted (e.g., CA, RCC, RCC Power Cord, aCM).

Table 35. Device deficiency reports by component M7 to M13

Component	Treatment (N=67)	Control (N=37)	Total (N=104)
Charging Antenna (CA)	10	11	21
Clinical Manager Software (aCM)	0	1	1
IPG	3	6	9
Lead	4	1	5
RCC/CA	1	0	1
Remote Control Charger (RCC)	11	6	17
RCC Power Cord	2	0	2
Total	**31**	**25**	**56**

For all DDs reported prior to Month 13, 151/159 (95.0%) were resolved in 72/74 (97.3%) of subjects reporting at least one DD in the study. The majority of DDs (148/159 (93.1%)) were

not related to an adverse event, and 154 of the 159 DDs (96.4%) were either not related to an AE or resolved via troubleshooting or no action was needed. Of the 11 DDs related to an AE, 7 were related to a Mild AE, 2 were related to a moderate severity AE, and 2 were related to a severe AE. **Table 36** reports the device deficiencies by component in each phase of the study.

Table 36. Device deficiency reports by component by study period

Component	Months 0 – 7 RCT	Months 7 – 13 Control Crossover	Months 0 -13
Charging Antenna (CA)	32	21	53
Clinical Manager Software (aCM)	3	1	4
IPG	14	9	23
Lead	20	5	25
RCC/CA	0	1	1
Remote Control Charger (RCC)	32	17	49
RCC Power Cord	2	2	4
Total	**103**	**56**	**159**

c) Effectiveness Results

Effectiveness – Month 7 (RCT)

The analysis of effectiveness was based on the ITT population at M7. The study met its primary effectiveness endpoint. In the ITT population, the Treatment group demonstrated a significantly higher AHI response rate (RR) of 58.2% (39/67) compared to 13.5% (5/37) in the Control group; a difference of 44.7% (95% CI: 28.5% to 60.8%; $p < 0.001$). See **Table 37.** Subjects in the Treatment group had 8.4 times higher odds to be responders than those in the Control group (95% CI: 2.8 to 25.2).

The Treatment group showed statistically significant differences from the Control group across the secondary endpoints, many of which are patient-reported measures. The secondary effectiveness endpoints were pre-defined to be tested in the following hierarchical order: ODI, ESS, FOSQ, PROMIS SDI and SRI, SF-6D, EQ-5D, and T90. The first five outcomes for ODI, ESS, FOSQ, PROMIS SDI and PROMIS SRI comparing Stimulation and Control groups were statistically significant and require no further adjustment for multiplicity. The remaining endpoints were not statistically significant; therefore, no inferential statistics such as confidence intervals are reported for these secondary endpoints.

A greater proportion of the Treatment group achieved a ≥50% reduction in ODI (56.7%) compared to the Control group (16.2%), with a between-group difference of 40.5% (95% CI: 23.7%, 57.3%). Similar results were observed for the proportion of subjects achieving a ≥

25% reduction in ODI, with 68.7% of the Treatment group responding versus 37.8% in the Control group, yielding a between-group difference of 30.8% (95% CI: 11.6%, 50.0%). Treatment led to a higher reduction in T90, which is the percentage of sleep time spent with oxygen saturation below 90%, with a between-group mean difference of -5.5 percentage points.

Sleep-related quality of life and daily functioning outcomes also favored the Treatment group. The overall FOSQ showed a mean improvement of 1.4 points over the Control group (95% CI: 0.6, 2.3). FOSQ includes items assessing difficulty concentrating due to being sleepy or tired, difficulty remembering things due to being sleepy or tired, and impairment in desire for intimacy or sex due to feeling sleepy or tired, all of which demonstrated improvements favoring the treatment group, consistent with results of the overall instrument.

The ESS score improved by 3.2 points in the Treatment group, exceeding the established MCID of 2 points, representing a reduction in daytime sleepiness. Compared to the change in the Control group, the Treatment group improved by 3.0 points (95% CI: 2.0, 5.0). Improvements in perceptions of sleep disturbances and sleep-related impairment over the past seven days were also seen in PROMIS SDI and SRI scores. The EQ-5D, a general measure of health-related quality of life, showed a modest improvement in the Treatment group of 3.2 points, whereas the Control group showed a decrease of 4.9 points. Furthermore, the clinician's impression of the subject's improvement in clinical condition compared to baseline, measured as a responder rate on the CGI-I scale, was observed in 56.3% of participants in the Treatment group versus only 8.6% in the Control group.

In contrast, the SF-36 Physical and Mental Component scores did not show any substantial differences between groups. This is likely due to the broad and general nature of the SF-36, which is not specific to OSA and may lack the sensitivity needed to detect treatment-related changes in this condition.

Overall, these results support the conclusion that the Treatment group experienced clinically meaningful improvements in OSA-related symptoms, sleep quality, and functional outcomes after 6 months of therapy relative to the Control group. See **Table 37**.

Table 37. Summary of Secondary Outcomes for OSPREY Study

Secondary Endpoint	Mean difference from Baseline at M7		
	Stimulation Group (N = 67)	Control Group (N = 37)	Difference[a] [Treatment-Control] [95% CI]
ODI RR ≥ 50%, %	56.7%	16.2%	40.5% (23.7%, 57.3%)
ODI RR ≥ 25%, %	68.7%	37.8%	30.8% (11.6%, 50.0%)
ESS, Mean (SD) *	-3.2 (5.02)	-0.5 (3.45)	-3.0 (-5.0, -2.0)
FOSQ, Mean (SD) *	1.8 (2.56)	0.08 (1.80)	1.4 (0.6, 2.3)
PROMIS SDI (T-score) Mean (SD) **	-6.6 (7.8)	-1.8 (6.0)	-6.6 (-9.6, -3.3)
PROMIS SRI (T-score) Mean (SD) ***	-7.3 (10.2)	-0.43 (6.8)	-6.4 (-10.4, -2.1)
SF-36 Physical component Mean (SD) ****	2.30 (6.11)	-0.15 (6.54)	1.6
SF-36 Mental component Mean (SD) ****	2.01 (8.83)	0.65 (7.25)	1.1
EQ-5D VAS *	3.2 (17.3)	-4.9 (14.8)	5.0
T90, Mean (SD) *	-5.3 (13.9)	1.6 (9.0)	-5.5
CGI-I RR, %	56.3%	8.6%	47.7%

* N = 66 for Stimulation group and N = 37 for Control group
** N = 62 for Stimulation group and N = 33 for Control group
*** N = 60 for Stimulation group and N = 31 for Control group
**** N = 62 for Stimulation group and N = 34 for Control group
[a] Confidence intervals are displayed only for the statistically significant endpoints as tested in a fixed-sequence (hierarchical) order to control for the multiple tests. Between group differences are calculated using Clopper-Pearson intervals for proportions and Hodges-Lehmann estimates of location shift for continuous variables.

Abbreviations: CGI = Clinical Global Impression; CI = Confidence interval; EQ-5D = EuroQoL 5-Dimension; ESS = Epworth sleepiness scale; FOSQ = Functional outcomes of Sleep Questionnaire; ODI = Oxygen desaturation index; RR = Responder rate; SD = Standard deviation; PROMIS = Patient Reported Outcomes Measurement Information System; SDI = Sleep Disturbance Index; SRI = Sleep Related Impairment SF-36 = 36-Item Short Form Survey; T90 = Sleep time with saturated oxygen index below 90%.

Effectiveness – Month 13

Following completion of the randomized controlled phase at Month 7, stimulation therapy was activated in subjects originally randomized to the Control group. Subjects originally randomized to the Treatment group continued stimulation and had received approximately

twelve months of therapy at the Month 13 visit. This delayed-activation study design permits assessment of durability of treatment effect in the early-activation cohort (original Treatment randomization) and assessment of onset of therapeutic benefit in the delayed-activation cohort (original Control randomization). Because all subjects were receiving therapy after Month 7, the Month 13 analyses are not intended for between-group comparison. There were no pre-specified statistical tests at this time point.

The primary endpoint of AHI responder rate as well as the secondary effectiveness endpoints are shown using data through Month 13 in **Table 38**.

In the early activation group, durability was demonstrated from Month 7 to Month 13. The median AHI improved over time from 34.3 (Baseline) to 11.6 (Month 7, -66%) to 11.0 (Month 13, -68%). The AHI responder rate of subjects with available data increased from 59.1% at Month 7 to 64.6% at Month 13. The ODI25 response rate increased from 69.7% at Month 7 to 80.0% at Month 13. All measures in the Treatment group were consistent or improved from Month 7 to Month 13.

In the delayed activation group, every available measure improved from Month 7 to Month 13 with therapy activated. The median AHI was little changed from 33.7 at Baseline to 34.5 at Month 7, but improved to 20.9 at Month 13. The AHI responder rate increased from 13.5% to 42.9%, and the ODI25 response rate increased from 37.8% to 65.7%. At Month 13, the ESS and FOSQ mean changes exceeded the MCID values of 2.

Table 38. Summary of Effectiveness Outcomes through Month 13

Primary and Secondary Endpoint through M13	Mean difference from Baseline			
	Early activation group (Treatment)		Delayed activation group (Control)	
	Month 7 N = 66	Month 13 N=65	Month 7 N=37	Month 13 N=35
AHI RR 50% to score < 20, %	59.1%	64.6%	13.5%	42.9%
AHI RR 50% to score < 20, % [WC]	58.2%	62.7%	13.5%	40.5%
Δ AHI, Mean (SD)	-14.9 (21.6)	-17.6 (15.3)	1.7 (16.7)	-10.6 (20.4)
ODI RR 50%, %	57.6%	63.1%	16.2%	48.6%
ODI RR 25%, %	69.7%	80.0%	37.8%	65.7%
ODI RR 25%, % [WC]	68.7%	77.6%	37.8%	62.2%
Δ ODI, Mean (SD)	-15.0 (21.5)	-17.7 (15.6)	1.6 (16.8)	-10.7 (20.3)
Δ ESS ≤ -2, %	63.6%	71.4%	32.4%	77.1%
Δ ESS ≤ -2, % [WC]	62.7%	67.2%	32.4%	73.0%
Δ ESS, Mean (SD)	-3.2 (5.02)	-3.7 (5.0)	-0.5 (3.45)	-3.6 (3.7)
Δ FOSQ ≥ 2, %	36.4%	54.0%	13.5%	42.9%

Primary and Secondary Endpoint through M13	Mean difference from Baseline			
	Early activation group (Treatment)		Delayed activation group (Control)	
	Month 7 N = 66	Month 13 N=65	Month 7 N=37	Month 13 N=35
Δ FOSQ ≥ 2, % [WC]	35.8%	50.7%	13.5%	40.5%
Δ FOSQ, Mean (SD)	1.8 (2.56)	2.6 (2.9)	0.08 (1.80)	2.1 (1.9)
Δ PROMIS SDI (T-score) Mean (SD)	-6.6 (7.8)	-7.4 (7.6)	-1.8 (6.0)	-8.8 (9.0)
Δ PROMIS SRI (T-score) Mean (SD)	-7.3 (10.2)	-9.4 (10.2)	-0.43 (6.8)	-9.1 (9.3)
Δ SF-36 Physical component Mean (SD)	2.30 (6.11)	2.36 (6.76)	-0.15 (6.54)	1.44 (5.42)
Δ SF-36 Mental component Mean (SD)	2.01 (8.83)	3.97 (9.55)	0.65 (7.25)	2.27 (9.54)
Δ EQ-5D VAS	3.2 (17.3)	2.5 (14.7)	-4.9 (14.8)	-1.7 (9.4)
Δ T90, Mean (SD)	-5.3 (13.9)	-5.0 (9.6)	1.6 (9.0)	-4.0 (16.0)
CGI-I RR, %	56.3%	58.7%	8.6%	48.6%

N denotes the number of subjects who completed the respective visit. The number of subjects with available data may differ by outcome. Subjects with missing data are not included except where specified.
WC = worst case, imputing all missing data as non-response.

Abbreviations: CGI = Clinical Global Impression; EQ-5D = EuroQoL 5-Dimension; ESS = Epworth sleepiness scale; FOSQ = Functional outcomes of Sleep Questionnaire; ODI = Oxygen desaturation index; RR = Responder rate; SD = Standard deviation; PROMIS = Patient Reported Outcomes Measurement Information System; SDI = Sleep Disturbance Index; SRI = Sleep Related Impairment SF-36 = 36-Item Short Form Survey; T90 = Sleep time with saturated oxygen index below 90%.

The durability of response can also be assessed by analyzing the patient-level responses in the Treatment group over time. Using the AHI Sher criteria in the N=65 subjects with data at both Month 7 and Month 13, there were 39 responders at Month 7. Of these, 32/39 (82.1%) maintained response at Month 13. In the same group of 39 responders, the median AHI at Month 7 was 7.2 which improved to 5.5 at Month 13. Therefore, there is a strong durability of response for subjects continuing therapy through Month 13.

Of the 26 non-responders at Month 7, 10 (38.5%) were responders at Month 13. Of these responders, the median AHI at Month 7 was 23.9 which improved to 9.2 at Month 13, whereas in the original 26 non-responders the median AHI at Month 7 was 30.6 and at Month 13 was 24.4.

For therapy utilization, the mean proportion of nights the therapy was used at least 4 hours was consistent in the Treatment group over time from 71.7% at Month 7 to 68.0% at Month 13. Similarly, the mean proportion of nights the therapy was used at least 4 hours in the delayed activation group at Month 13 was 70.6%. On nights when the device was used, the mean hours of use were 6.2 (Treatment Month 7), 6.3 (Treatment Month 13), and 6.0 (delayed activation group Month 13).

d) **Pediatric Extrapolation**

Implantation in this patient population has not been studied and therefore is not recommended in patients less than 22 years of age. Existing clinical data was also not leveraged to support approval of a pediatric patient population.

ix. Subgroup Analyses and Additional Analyses

For the primary effectiveness endpoint, across subgroups, the Treatment group consistently exhibited higher response rates compared to the Control group. Comparisons within sex (male versus female), age group (< 65 years versus ≥ 65 years), race group (Hispanic or Latino versus Non-Hispanic or Latino), baseline OSA severity (moderate versus severe), BMI (< 32 kg/m^2 versus ≥ 32 kg/m^2) and tonsil grading scale (grade 0 versus grade 1 versus grade 2) did not demonstrate a clear association with treatment response. See **Table 39**. This supports the generalizability of the treatment effect across a diverse patient population.

Table 39. Subgroup Analysis of Primary Efficacy Endpoint: AHI Response Rate at Month 7 by Treatment Group

	Stimulation (N = 67) n/N (%)		Control (N = 37) n/N (%)		Difference in Proportion and 95% Confidence Interval	
Sex						
Female	10/18	(55.6%)	1/10	(10.0%)	45.6%	(16.0%, 75.1%)
Male	29/49	(59.2%)	4/27	(14.8%)	44.4%	(25.2%, 63.6%)
Age						
<65	31/54	(57.4%)	4/31	(12.9%)	44.5%	(26.8%, 62.2%)
>=65	8/13	(61.5%)	1/6	(16.7%)	44.9%	(5.0%, 84.7%)
Ethnicity						
Hispanic or Latino	8/10	(80.0%)	1/8	(12.5%)	67.5%	(33.7%, 100.0%)
Non-Hispanic or Latino	31/56	(55.4%)	4/29	(13.8%)	41.6%	(23.5%, 59.6%)
NOT REPORTED	0/1	(0%)	0/0	(0%)	0%	(0%, 0%)
Body Mass Index						
< 32	26/44	(59.1%)	4/21	(19.0%)	40.0%	(17.8%, 62.2%)
>= 32	13/23	(56.5%)	1/16	(6.3%)	50.3%	(26.8%, 73.7%)
Baseline OSA Severity						
Moderate	16/27	(59.3%)	4/14	(28.6%)	30.7%	(0.6%, 60.7%)
Severe	23/40	(57.5%)	1/23	(4.3%)	53.2%	(35.7%, 70.6%)

	Stimulation (N = 67) n/N (%)	Control (N = 37) n/N (%)	Difference in Proportion and 95% Confidence Interval
n: Number of subjects with response, N: Total number of randomized subjects qualifying to provide information to the endpoints			

a) Ancillary Analyses

The Obstructive Apnea Index and the Arousal Index were computed as ancillary endpoints. The rate of obstructive apneas was reduced by 89.1% (based on the median value of 5.5 at baseline and 0.60 at M7) in the Treatment group. Additionally, the Treatment group demonstrated a 44.0% reduction of sleep interruptions, based on the median value of 54.7 at baseline and 30.7 at M7.

x. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. None of the pivotal study clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Anesthesiology and Respiratory Therapy Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

In the pivotal OSPREY study, aura6000™ system therapy provided the majority of subjects with clinically meaningful reductions in the severity of their obstructive sleep apnea and improvements in their quality of life. At Month 7, 58.2% (39/67) of Treatment subjects achieved a clinically meaningful reduction in AHI (Sher criteria) from baseline compared to 13.5% (5/37) of Control subjects. Secondary endpoints provided additional validation of therapy effectiveness, including ODI responder rate and several measures of quality of life. Durability of the benefit achieved with aura6000™ device was demonstrated in OSPREY,

with 64.6% of subjects originally randomized to treatment demonstrating a significant reduction in AHI at Month 13.

Overall, the clinical studies have demonstrated a reasonable assurance of effectiveness for use in treating moderate to severe obstructive sleep apnea in adult patients who have failed or were unwilling to use PAP treatment.

B. Safety Conclusions

The risks of the device are based on data collected from multiple clinical studies conducted to support PMA approval as described above. In the pivotal OSPREY study, the majority of TEAEs were mild in severity, with similar overall rates between the Treatment and Control groups. From implant through M7, the most commonly reported TEAE was headache, occurring at nearly identical rates in both groups (Treatment: 16.4%; Control: 16.2%). Other frequent TEAEs in the Treatment group included implant site pain (11.9%), dysphagia (10.4%), COVID-19 (9.0%), and ear pain (7.5%). In the Control group, the most frequently reported TEAEs, aside from headache, included oropharyngeal pain (10.8%), as well as ear pain, glossodynia, and implant site pain (each reported in 5.4%). Stimulation-related TEAEs were infrequent but occurred more often in the Treatment group (19.4%) compared to the Control group (0%) through Month 7.

From Month 7 to Month 13, the TEAE severity profile was consistent with the randomization phase of the study, with most of the TEAEs classified as mild. The most common (> 5% of subjects reporting) of the TEAEs reported in this timeframe was Nasopharyngitis (5.8%) with no other events being seen in > 5% of subjects.

Through Month 13, a total of 11 (10.6%) subjects underwent a device-related reoperation (classified as serious adverse device effects), including 5 replacements of IPG and/or lead, 4 IPG pocket revisions, 4 explants, and 1 lead repositioning.

C. Benefit-Risk Assessment

Clinical data from the OSPREY pivotal study, supported by long-term data from prior aura6000™ investigations, demonstrates that the aura6000™ system provides statistically and clinically significant improvements in obstructive sleep apnea (OSA) severity and related symptoms. Improvements in AHI, ODI, ESS, and FOSQ observed at Month 7 were maintained through Month 13, indicating sustained benefit during the first year of therapy. Additional assurance of the long-term durability of aura6000™ therapy through 5 years is demonstrated via the prior clinical experience with the device (THN3).

The safety profile of the aura6000™ device is consistent with an implantable neurostimulation device used in patients with moderate to severe OSA. Most adverse events were mild and transient. No unanticipated adverse device effects, or deaths were reported under the prespecified, IDE-approved definitions applied during the study. As with other surgically implanted HGNS systems, a subset of subjects required revision procedures

following implantation. These procedures were infrequent, varied in cause, and resolved without long-term sequelae. Comprehensive information regarding the frequency, type, and timing of these surgical interventions is provided in the Safety and Surgical Interventions sections of this SSED.

Taken together, the totality of clinical evidence demonstrates the device's superiority over Control in significantly improving both objective measures of sleep-disordered breathing, such as AHI and ODI, and patient-reported outcomes, including ESS and FOSQ. These benefits are not only sustained over 13 months of therapy based on available data but may persist for up to 5 years. Importantly, the magnitude and durability of these improvements outweigh the risk of surgical intervention for device explant or revision. When considered alongside the potential need for revision surgery, the therapeutic benefits of the aura6000™ system outweigh its associated risks for appropriately selected patients who decline or cannot tolerate PAP therapy.

D. Patient Perspectives and Satisfaction

Patient perspectives were evaluated through validated questionnaires assessing sleep-related quality of life and functional outcomes. As described in the Secondary Effectiveness Endpoints (Table 37), statistically significant improvements were observed in the Treatment group compared to Control for FOSQ, ESS, PROMIS SDI, and PROMIS SRI

- **Functional Outcomes of Sleep Questionnaire (FOSQ-10)**: This 10-item instrument measures the impact of excessive sleepiness on functional activities of daily living, including activity level, vigilance, intimacy and sexual relationships, general productivity, and social outcomes. The Treatment group showed a median improvement of 1.25 points from baseline to M7 (95% CI: 0.83, 1.83), compared to 0.17 points in the Control group (95% CI: -0.87, 0.33), with a between-group difference of 1.4 points (95% CI: 0.6, 2.3). At M13, both groups demonstrated improvements after receiving therapy (Treatment: 2.33 points; Control: 1.67 points).

- **Epworth Sleepiness Scale (ESS)**: This 8-item questionnaire assesses daytime sleepiness by measuring the likelihood of dozing off in various situations. The Treatment group demonstrated a median reduction of -3.5 points from baseline to M7 (95% CI: -5.0, -2.0), exceeding the minimal clinically important difference (MCID) of 2 points, compared to no change in the Control group (median: 0.0; 95% CI: -2.0, 0.0). The between-group difference was -3.0 points (95% CI: -5.0, -2.0). At M13, both groups showed similar reductions (Treatment: -4.0 points; Control: -3.0 points).

- **PROMIS Sleep Disturbance Index (SDI)**: This instrument assesses self-reported perceptions of sleep quality, sleep depth, and restoration associated with sleep, including perceived difficulties and concerns with getting to sleep or staying asleep, as well as perceptions of the adequacy of and satisfaction with sleep over the past seven days. The

Treatment group showed a greater reduction in mean T-scores (-6.6 ± 7.8 points) compared to Control (-1.8 ± 6.0 points) at M7. At M13, both groups demonstrated similar improvements (Treatment: -7.4 ± 7.6; Control: -8.8 ± 8.9).

- **PROMIS Sleep-Related Impairment (SRI)**: This instrument focuses on self-reported perceptions of alertness, sleepiness, and tiredness during usual waking hours, and the perceived functional impairments during wakefulness associated with sleep problems or impaired alertness. The Treatment group demonstrated a greater reduction in mean T-scores (-7.3 ± 10.2 points) compared to Control (-0.4 ± 6.8 points) at M7. At M13, improvements were similar between groups (Treatment: -9.4 ± 10.2; Control: -9.1 ± 9.3).

- **SF-36 (Medical Outcomes Study 36-Item Health Survey Short Form)**: This general health-related quality of life instrument assesses physical and mental health across eight domains. The SF-36 physical and mental component scores did not show statistically significant differences between groups at M7. As a broad, general health measure not specific to OSA, the SF-36 may lack sensitivity to detect OSA-specific treatment effects.

- **EQ-5D-5L (EuroQol 5-Dimension 5-Level)**: This generic quality of life instrument evaluates health status across five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). The EQ-5D assessments did not demonstrate statistically significant differences between groups at M7.

E. Patient Satisfaction: At the M13 visit, 75% of Treatment subjects reported being satisfied or very satisfied with the therapy, and 82.5% indicated they would recommend the therapy to a friend with similar OSA symptoms.Overall Conclusions

The totality of the evidence provided in this PMA application provides reasonable assurance that the aura6000™ system is safe and effective for treating moderate to severe OSA, based on the observed improvements in sleep-disordered breathing, oxygenation, and quality of life, and outweighing the risks identified in the safety profile of the device.

XIII. CDRH DECISION

CDRH issued an approval order on March 18, 2026. The final conditions of approval are cited in the approval order are described below.

1. **Extended Follow-up of the Premarket Cohort (OPSPREY Study):** This study will be conducted as a multi-center, prospective, observational, open-label, long-term follow-up of subjects who completed the M13 visit of the OSPREY clinical trial. This study is designed to evaluate the long-term safety and efficacy of the aura6000™ system in up to 150 subjects previously implanted under the premarket study, with follow-up extending to 5 years post-surgery (approximately 60 months on therapy for the active group and 4.5 years on therapy for the control group. The primary safety objective is to evaluate long-term device-related and procedure-related adverse events, with relationship to procedure

and device. The primary efficacy objective is to evaluate change in AHI (Apnea Hypopnea Index) relative to the pre-therapeutic baseline in subjects implanted with the aura6000™ system annually based on home sleep test (HST) and/or polysomnography (PSG) data with success criteria defined as achieving a 50% responder rate in evaluable subjects for AHI responder criteria (≥50% reduction and AHI <20). Secondary assessments include changes in sleep-disordered breathing and quality of life outcomes from pre-therapeutic entry to annually thereafter through validated instruments including decrease in ODI between pre-therapeutic timepoint and annual visit, change in ESS (Epworth Sleepiness Scale) between pre-therapeutic timepoint and annual visit, change in FOSQ (Functional Outcomes of Sleep Questionnaire) between pre-therapeutic timepoint and annual visit, Clinical Global Impression Severity (CGI-S) at pre-therapeutic timepoint, and Clinical Global Impression Improvement (CGI-I) annually thereafter. All adverse events will be summarized descriptively, and subjects will undergo biannual impedance checks to assess IPG function.

2. **New Enrollment Study (Post-Approval Study):** This study will be initiated upon commercial introduction of the device as a multicenter, prospective, single-arm, post-approval study to demonstrate the long-term safety and effectiveness of the device in treating subjects diagnosed with moderate to severe obstructive sleep apnea (OSA), defined as an apnea-hypopnea index (AHI) of ≥15 and ≤65, who have failed, do not tolerate, or are ineligible to be treated with current standard of care treatments such as positive airway pressure (PAP), oral appliances (e.g., mandibular advancement device), or pharmacotherapy. The study is planned to enroll to a target of 160 implanted subjects at a minimum of 10 US sites, with baseline evaluation, device implantation, and therapy activation at 4 to 6 weeks post-implantation. Subjects will then have follow-up visits at 6 months, 12 months, and every 6 months thereafter for up to 5 years. Safety events will be assessed through collection of all device-related and procedure-related adverse events (AEs) or serious adverse events (SAEs) including device explants due to infection, malfunction, or repositioning requiring surgery, that will be captured at all scheduled and unscheduled visits. The safety of the device will be monitored relative to performance observed in the premarket experience from the OSPREY study including the rate of device-related SAEs of 10.3% through Month 13. The primary efficacy objectives include therapy efficacy measured by improvement in OSA severity (AHI) using annual in-lab polysomnography at years 1, 2, 3, 4, and 5, with success criteria defined as achieving a 50% responder rate in evaluable subjects for AHI responder criteria (≥50% reduction and AHI <20). Secondary endpoints will include ODI responder rate (≥50% reduction from baseline), subject satisfaction, change in Functional Outcomes of Sleep Questionnaire (FOSQ), change in Epworth Sleepiness Scale (ESS), Clinical Global Impression Improvement (CGI-I), and therapy utilization metrics. With 80% statistical power and a 5% one-sided significance level, the study aims to reject the null hypothesis that the percentage of responders in evaluable subjects at Month 60 will be less than 50%. This study will continue to follow participants for up to 5 years, with endpoints assessed and reported yearly till the 60-month mark, and subjects will undergo biannual impedance checks to assess IPG function and battery status.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820), which was in effect at the time of the inspection. As of February 2, 2026, the revised part 820, referred to as the Quality Management System Regulation (QMSR), is effective.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.