# Nyxoah

*– Shaping the Future of Obstructive Sleep Apnea Therapy –*

**Finance Avenue – 16 November 2024**

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# Experienced Board and Management Team

## Robert Taub
Founder, Chairman

- Serial entrepreneur in the pharmaceutical and medical fields.
- Co-founded and co-managed Octapharma – Human plasma protein company.
- Founded and managed Omrix Biopharmaceuticals – NASDAQ IPO, followed by the acquisition by J&J.
- Early investor and chairman of Neuroderm, a Parkinson's disease pharmaceutical company – IPO on NASDAQ and later sale to Mitsubishi-Tanabe.

## Olivier Taelman
Chief Executive Officer

- Experienced Medtech leader.
- 7 years in pharmaceutical healthcare at Eli Lilly and Sanofi Aventis leading specific Business Units.
- 18 years within the field of Medtech neuromodulation at Medtronic, managing EMEA at Stryker NeuroVascular and serving a neuromodulation company Nevro where he was responsible for building the European business during the successful NASDAQ IPO.
- Joined Nyxoah in July 2019 as Chief Operating and Commercial Officer, subsequently being appointed as CEO in November 2019.

## John Landry
Chief Financial Officer

- 20 years of financial leadership experience in the healthcare and medtech sectors.
- Proven track record of driving growth and operational efficiency in public and private companies.
- Expert in executing financial strategies that support significant revenue growth and market share expansion in the U.S. market.



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# Nyxoah’s Blueprint for Success

- $10 Billion US HGNS Market Opportunity
- 8% Market Penetration
- Established HGNS Reimbursement

Breakthrough Treatment For Obstructive Sleep Apnea With Unique Bilateral Mode of Action

Compelling Clinical Evidence Through DREAM IDE Study Demonstrating Safety and Efficacy of Genio® Therapy

Proof-of-Concept European Commercialization

On the Verge of FDA Approval with US Commercialization Planned in Early 2025

# The Nyxoah Journey
*Key company milestones*

**2016**
**VC Investment**
Gilde-Led Financing

**Strategic Investors**
Cochlear- and Resmed- Led Financings

**Euronext IPO**
€ 85M Raised

**NASDAQ IPO**
$98M Raised

ATM - $6M funding
Private Placement - $15M

Equity Raise: €45.9M

EIB: €37.5M Loan Facility Agreement

ATM: $27M funding

**2012 – 2016**

- 2012 – First-in-Man Study
- 2014 – Proof-of-Concept Study
- 2016 – Genio Invention

**2017 – 2020**

- 2017 & 2018 – BLAST OSA Clinical Study
- 2019 – CE Mark Approval

**2020**

- DREAM IDE Pivotal Study Approval

**2021**

- Dedicated DRG in GER & CH
- EU Commercialization
- CCC: EU Label Expansion / FDA Break-Through Designation

**2022**

- Commercialization in Spain & Finland
- ACCCESS IDE Approval
- Genio 2.1 CE Mark

**2023**

- DREAM Enrolments Completion
- ACCCESSS First Implants
- PMA Modules 2 & 3 Submission
- Partnership Agreement with ResMed in Germany

**2024**

- DREAM 12M data
- PMA Module 4 Submission
- DREAM Data Presentation at ISSS Congress



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# Large and Underpenetrated Global OSA and HGNS Market Opportunity

## Worldwide Obstructive Sleep Apnea Prevalence

**936 Million**

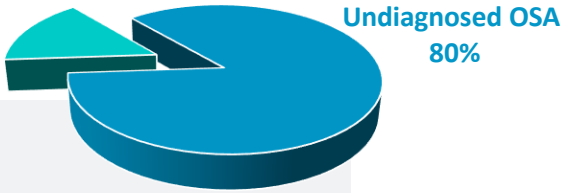
- 936M individuals (30-69 year) are estimated to suffer from OSA[1]

**425 Million**

- 425M suffer from moderate to severe OSA, requiring therapy[1]
- Increasing prevalence of OSA due to rise in obesity
- Significant OSA comorbidities, including cardiovascular disease and type II diabetes

**20%**

- Only 20% OSA patients are diagnosed[2]




## Hypoglossal Nerve Stimulation Market Opportunity

**>1 million eligible annually in key geographies**

- US: 510,000 eligible patients annually
- Europe: 500,000 eligible patients annually

**~85,000 received HGNS as treatment**

- First HGNS CE-Mark approval in 2010 – FDA authorization in 2014
- Low awareness on neurostimulation as an OSA solution
- Limited reimbursement

**+67% CAGR HGNS revenue 2017 – 2023[3]**

- Endorsed by the global sleep and ENT medical communities
- Accepted by US/EU payors
- Embraced by OSA patient association groups

1. Benjafield, Adam V et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med 2019
2. Harvard Medical School Division of Sleep Medicine, The Price of Fatigue - The surprising economic costs of unmanaged sleep apnea, December 2010
3. Presents annual revenue growth for Inspire Medical. Inspire Medical corporate presentation – February 2024



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# Existing Conventional Therapeutic OSA solutions

*Need for therapeutic alternatives to existing solutions*

## A Variety of Options are Available for the Treatment of OSA

### Positive Airway Pressure (PAP)

- First line therapy for 80% of OSA patients[14]
- The PAP system is comprised of a machine pushing air at a constant or automated pressure and a mask (oral or facial) that the patient needs to put on his face and wear all night
- CPAP (Continuous Positive Airway Pressure) is the most common type of Positive Airway Pressure (PAP) therapy

**CPAP therapy compliance is a major issue for some patients[15]**

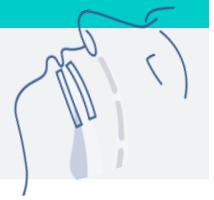
CPAP non-compliance has been estimated to be between 29% and 83%[16, 17, 18]

### Oral devices / Mandibular Advancement Devices (MAD)

- Looking similar to orthodontic retainers
- Help the airway passage to remain open by bringing the jaw forward

**MAD therapy has multiple limitations**

- More suitable for mild to moderate OSA
- Non predictive therapy efficacy
- Low therapy efficacy rate: 21%[19] to 50%



### Surgery

In patients having difficulty with other treatments, surgical procedures for the nose (e.g. nasal), throat (e.g. palate, tonsils, uvula) or mandible can be a beneficial alternative.

**Traditional surgery remains a last resort option**

- Highly invasive
- Success rate from 30% to 60%[20]
- High incidence of side effects

*A patient using his/her CPAP 4H/night, 5 days/week is considered compliant during the first 90 days of Therapy – Medicare Revised Guidelines for CPAP Therapy in the home


14. Harvard Medical School Division of Sleep Medicine, The Price of Fatigue - The surprising economic costs of unmanaged sleep apnea, December 2010
15. Sunwoo BY, Light M, Malhotra A. Strategies to augment adherence in the management of sleep-disordered breathing. Respirology 2019
16. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am. Rev. Respir. Dis. 1993; 147: 887–95.
17. Sawyer AM, Gooneratne NS, Marcus CL, Ofer D, Richards KC, Weaver TE. A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. Sleep Med. Rev. 2011; 15: 343–56
18. Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. Proc. Am. Thorac. Soc. 2008; 5: 173–8
19. Hoffstein, V, Review of oral appliances for treatment of sleep-disordered breathing. Sleep Breath 2007; 11(1): 1-22
20. Shah, Janki, et al; American Journal of Otolaryngology (2018). Uvulopalatopharyngoplastyvs CN XII stimulation for treatment of obstructive sleep apnea: A single institution experience

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# Genio® Therapy

*A breakthrough solution with unique bilateral mode of action*

## Implantable Stimulator

- Lead-less, battery-free stimulator inserted through a single incision
- Delivers bilateral hypoglossal nerve stimulation, which contracts the genioglossus muscle to maintain an open airway in any sleep position
- Genio implant not visible with full-body MRI compatibility at 1.5T and 3.0T

## Wearable

- Externally powers the stimulator
- Conduit for feature upgrades without the need for additional procedures to upgrade or replace a generator

## Patient App

- Puts control in the hands of patients (within limits set by a health care professional)
- Provides feedback on therapy usage





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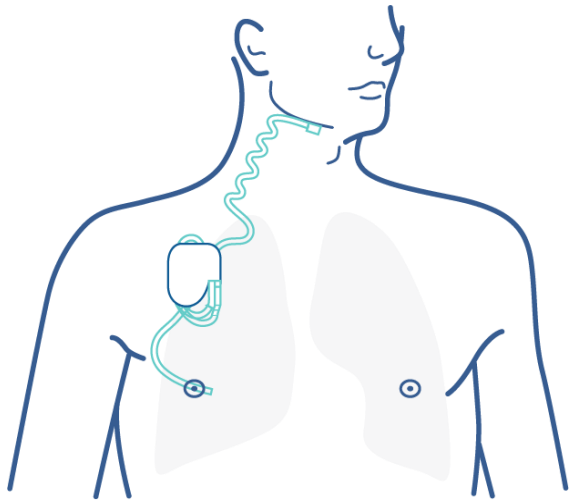
# A New Choice in HGNS Therapy

- Over 20% of HGNS eligible patients refuse pacemaker-based therapies due to:
  - Multiple incision procedure
  - Need for additional surgical reintervention upon battery depletion
  - Leads and IPG inserted in the body
  - MRI compatibility restrictions
  - Potential limitations in sleep positions





Source: Wall Street and Company research

# HGNS Market – Germany
*A high-potential, underpenetrated market opportunity*

## Market

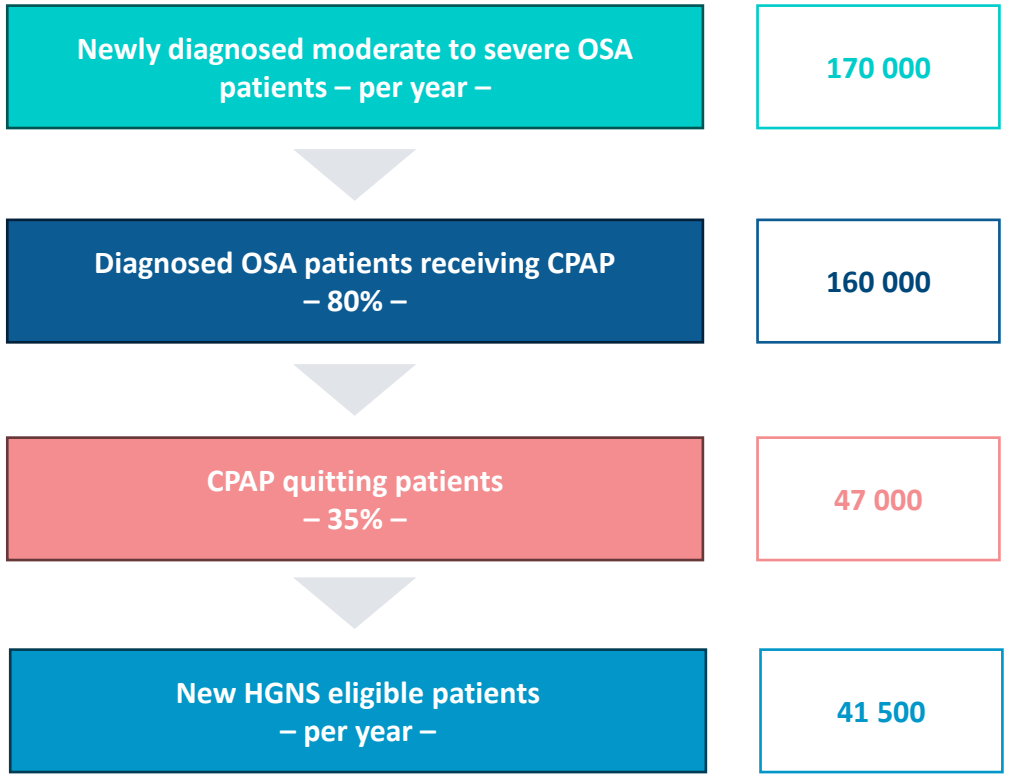
- 2nd largest HGNS market after the United States
- CE Mark in 2019 > Dedicated German DRG since late 2021

| Diagnosed moderate to severe OSA patients | 2023 |
|---|---|
| Prevalence | 2 500 000 |
| • Treated – CPAP gold standard | 1 100 000 |
| • Untreated | 1 400 000 |

| | 2023 |
|---|---|
| Total HGNS Patients | 850 |
| HGNS Market Penetration | 2% |

Source: ResMed GmbH

## HGNS eligible patients' annual incidence



# Germany Commercial Proof of Concept
*Genio driving growth of the HGNS market*

## HGNS Centers of Excellence

**Nyxoah focus on Tier 1 accounts**

- 65 HGNS implanting accounts in Germany
- Selectively target physicians with high outcomes potential
- Top 10 accounts amount for > 50% implants
- Genio embraced by 9 out of 10 top implanting accounts

## Genio Sleep Hubs

**Streamline referral pathway**

- Focus on screening and qualifying patient candidates
- Build an OSA ecosystem with strong partnership between sleep hubs & ENT centers
- 15 active sleep hubs in 2024 > 25 by end 2025

## Focused DTC efforts

**Driving patients to the Genio funnel**

- Focus DTC efforts supporting sleep hubs and Tier 1 accounts
- Reduce the ENT screening burden by increasing qualification yields
- Exclusive partnership agreement with ResMed Germany

- Nyxoah driving HGNS market growth in Germany
  - INSP low single digit growth
  - NYXH 30% growth

- 25% overall market share only 24 months after German launch



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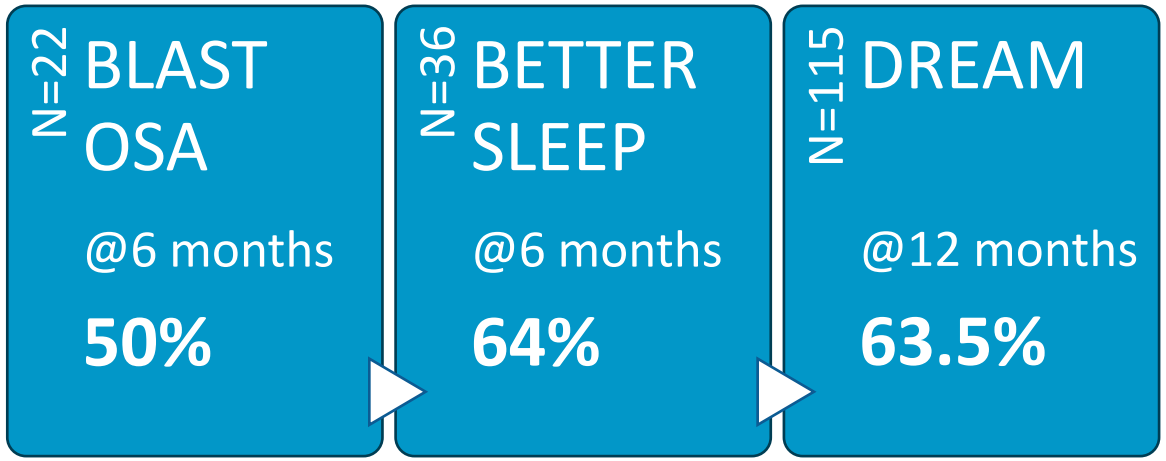
# Clinical Strategy Overview

## Growing Body of Clinical & Real-life Evidence

| | |
|---|---|
| BLAST OSA | CE Mark |
| BETTER SLEEP | CCC label – Europe |
| ElISA | Long term data – Europe |
| DREAM | IDE Pivotal Study – US |
| ACCCESS | CCC IDE Pivotal Study – US |
| Commercial | European sales |

**~500 patients implanted and >125 doctors trained with Genio in clinical studies and commercially**

## AHI Responder Rates



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# DREAM U.S. Pivotal Study
*Study design & endpoints*

## Design

- n=115
- Pivotal, multi-center, prospective, open-label study
- Safety and performance of bilateral HGNS system in adult patients
- **Supine sleep time required: ≥60 minutes at 12 months**
- **AHI range between 15 and 65, BMI<32**

## Baseline Characteristics

- Mean Baseline AHI: 28.0 events/h
- Mean Baseline ODI: 27.0 events/h
- Mean BMI: 28.5 kg/m$^2$

## Endpoints

**Efficacy**

- Co-Primary – AHI responder rate, per the Sher criteria, at 12 months
- Co-Primary – ODI responder rate at 12 months
- Secondary – Median reduction in AHI from baseline to 12 months

**Safety**

- Incidence of device-related serious adverse events (SAEs)*
- Adjudicated by an independent clinical events committee (CEC)

### AHI responder – Sher criteria
- AHI reduction of at least 50% from baseline on the 12-month PSG
  ***AND***
- AHI score of less than 20 events per hour on the 12-month PSG

### ODI responder
- ODI reduction of at least 25% from baseline on the 12-month PSG

*All assessments from consent (safety) or baseline (efficacy) to 12 months post-implant



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# DREAM Study

*DREAM study achieved primary endpoints*

## Achieved Co-Primary Efficacy Endpoints on an ITT basis

- AHI Responder Rate – 63.5% (p=0.002)
- ODI Responder Rate – 71.3% (p<0.001)

| Safety Set – ITT | Responder Rate M12 | *p* value |
|---|---|---|
| AHI4 | 63.5% (73/115) | 0.002 |
| ODI4 | 71.3% (82/115) | < 0.001 |

| Full Analysis – m-ITT | Responder Rate M12 | *p* value |
|---|---|---|
| AHI4 | 66.4% (73/110) | < 0.001 |
| ODI4 | 74.5% (82/110) | < 0.001 |

| Per Protocol – PP | Responder Rate M12 | *p* value |
|---|---|---|
| AHI4 | 81.8% (72/88) | 0.001 |
| ODI4 | 92.0% (81/88) | < 0.001 |

## Achieved Safety Endpoint

- Safety results compare favorably vs. standard of care*
- All events were adjudicated by an independent Clinical Events Committee (CEC)
- 11 SAEs in ten subjects resulting in an SAE rate of 8.7%
  - **3 device-related adverse events**

| SAE | Related to Device | Related to Procedure | Unrelated to Device and/or Procedure |
|---|---|---|---|
| Asthenia and Hypoesthesia | | | 2 |
| Atrial Fibrillation | | | 1 |
| **Device Dislocation** | **2** | | |
| **Device Extrusion** | **1** | | |
| Left Bundle Branch Block | | 1 | |
| Dysphagia | | 2 | |
| Epistaxis | | 1 | |
| Incision Site Hematoma | | 1 | |
| **TOTAL: 11** | **3** | **5** | **3** |

*For illustrative purposes only. DREAM did not include a head-to-head comparison to standard of care treatments. Stats are based on the Company's review of third-party outcomes, and caution should be exercised when comparing results from unrelated studies or sources.

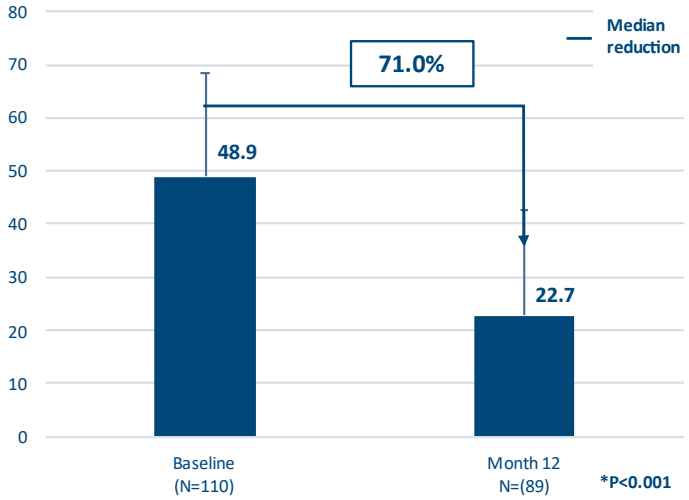
# Key Differentiating Data vs. Unilateral HNS

## AHI improvements are independent from the sleep position

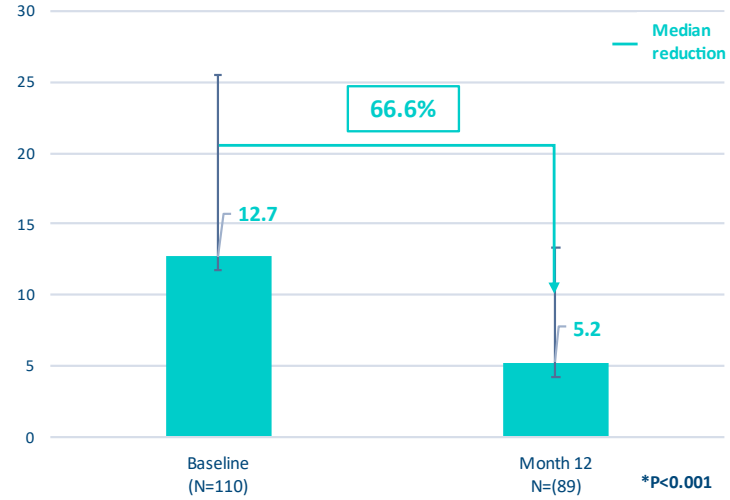
- Median AHI change of 71.0% in supine sleep
- Median AHI change of 66.6% in non supine sleep
- Median AHI change of 70.8% in all positions

**Submitted a unique label claim that Genio is usable in any sleeping position**

### Mean change in SUPINE AHI*




### Mean change in NON-SUPINE AHI*

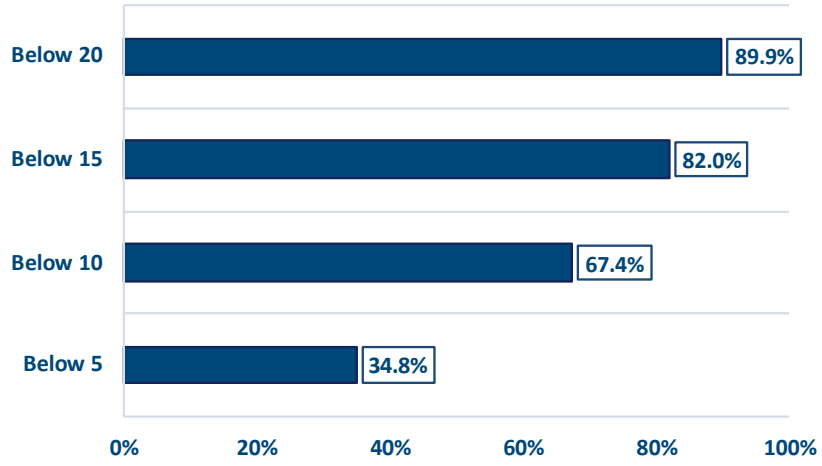



## Therapy impact on AHI at 12 months

- 82.0% patients had an AHI below 15 at 12 months
- 67.4% patients had an AHI below 10 at 12 months

**Patients with AHI below 15 have equivalent cardiovascular risks to the non-OSA population**

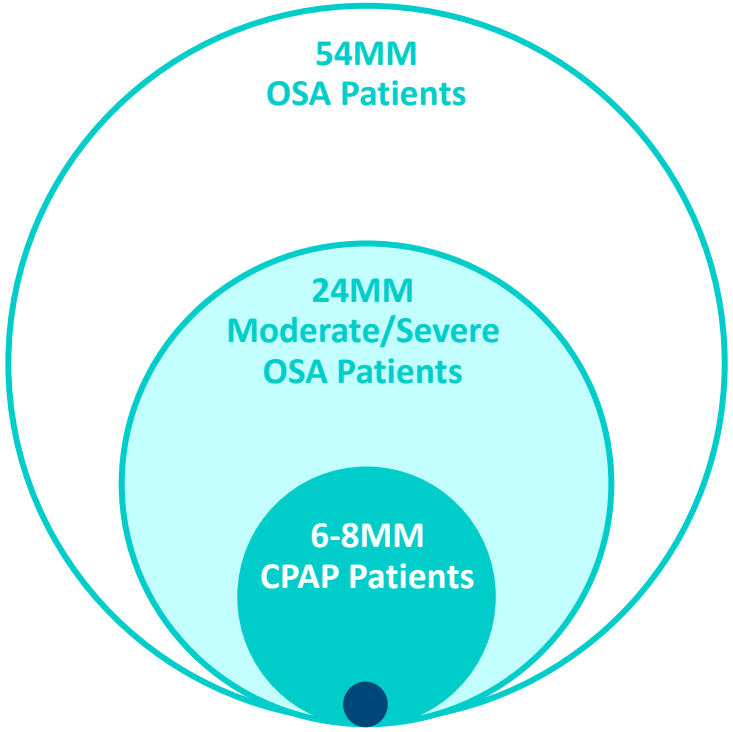
### AHI at 12-M visit – % Patients



# The US Market Opportunity for Hypoglossal Nerve Stimulation

*Currently, 97% of HGNS revenue is generated in the U.S.*

## Many More OSA Patients Need Help

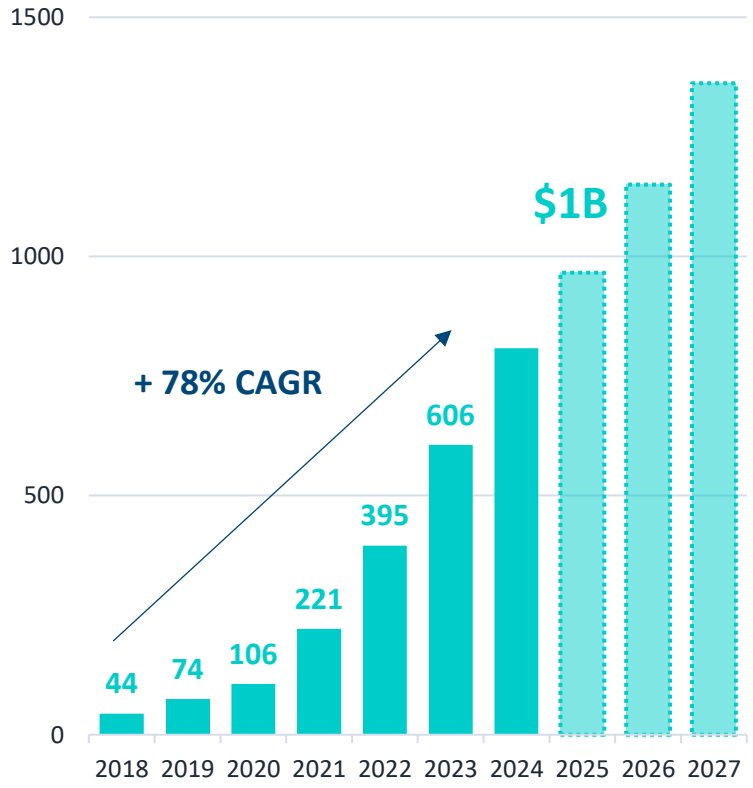



**85K HGNS Implants To Date**

## HGNS Has Not Yet Focused On Where OSA Patients Are

| Specialty | # of US Clinicians | Current HGNS Industry Focus |
|---|---|---|
| Primary Care Providers | 295,000 | Low |
| Pulmonologists (primary specialty) | 4,900 | Low |
| Sleep Doctors (at 2,500 centers) | 7,500 | Low to Moderate |
| Sleep-Focused ENT Surgeons | 1,300 | High |

## Market Poised For Robust Growth




Sources: 1. Benjafield, Adam V et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med 2019. 2. ResMed, 3. Inspire company reports, 4. Associated Professional Sleep Societies, 5. American Medical Association Physician Professional Database 2022.



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# US Commercialization Strategy
*Make Sleep Simple*

## Smart Follower

### Break the HGNS monopoly

- Targeting the now firmly established subspecialty of sleep surgeons – a highly concentrated group in ENT growing their practices through device-forward treatment
- Leveraging business processes already streamlined at high-volume physician offices with referral pathways from sleep centers
- Payers acknowledge the role of hypoglossal nerve stimulation in the OSA treatment algorithm and the supporting evidence around category outcomes

## Patients at the Center

### Make Genio the patient's preference

- Bilateral stimulation to address both sides of the genioglossus muscle to maintain an open airway regardless of sleep position
- Lead-less, battery-free implant inserted via a single incision that does not require follow-on procedures to replace generators
- Genio device not visible after implant
- Full-body MRI compatible up to 3T
- Patient app that empowers patient to adjust therapy and see their treatment success

## Playbook for Scalability

### Carve a fast track to profitability

- Focus on top-tier, geographically concentrated ENT accounts, and strengthening their sleep referral network
- Target DTC at critical points along the patient journey
- Launch with sustainable processes that make business simple for stakeholders, then add geographies following initial success
- Complement prior work done in coding and payment with coverage support via prior authorization and interim codes until a new code is established



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# Genio US Launch Success Factors

Experienced talent with track records of success and the right mindset—with US-based leadership

Commercial launch team focused on selected geographies, bolstered by market access, marketing, and commercial operations expertise

Developing sustainable traction in the US as a premium option to take share and accelerate market growth

Keeping the patient at the center to ensure the right patient gets the right therapy for the best outcomes

# 2024 – 2025 Key Milestones


**CLINICAL EVIDENCE**

- **DREAM** 12M data

**REGULATORY**

- All PMA Modules Submitted
- Interactive Review with FDA
- Expected FDA Approval of Genio

**COMMERCIAL**

- US Commercial Launch Readiness
- Planned US Launch
- Further Geographic Expansion

**LABEL EXPANSION**

- Complete Concentric Collapse in the US
- Ansa Cervicalis Stimulation



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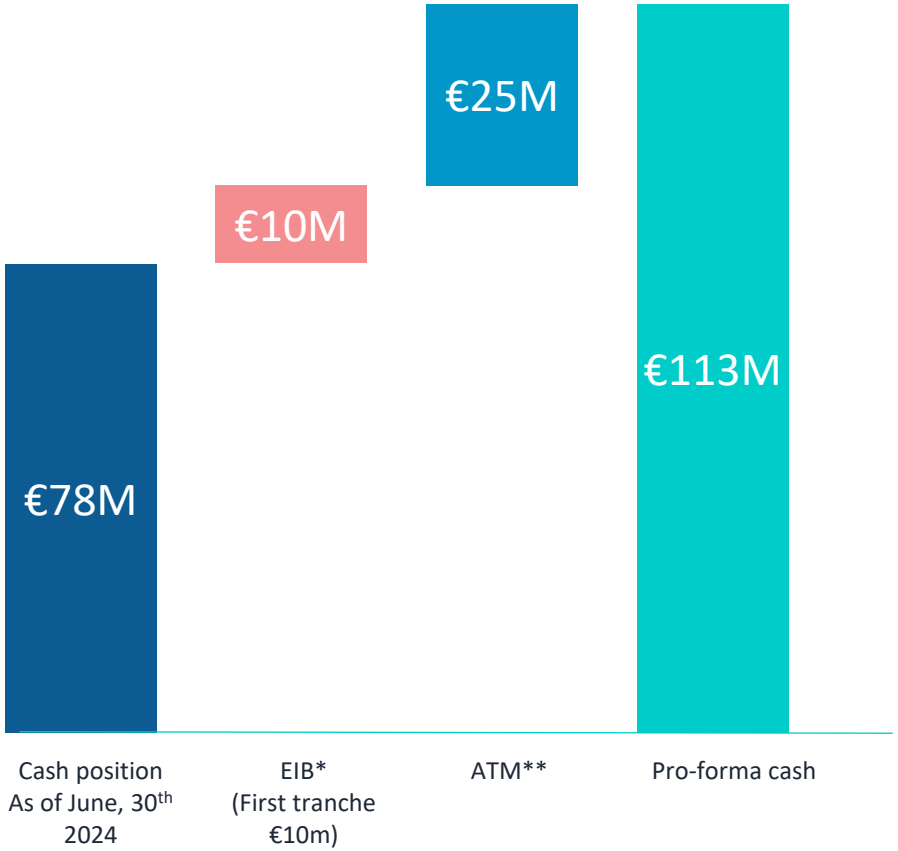
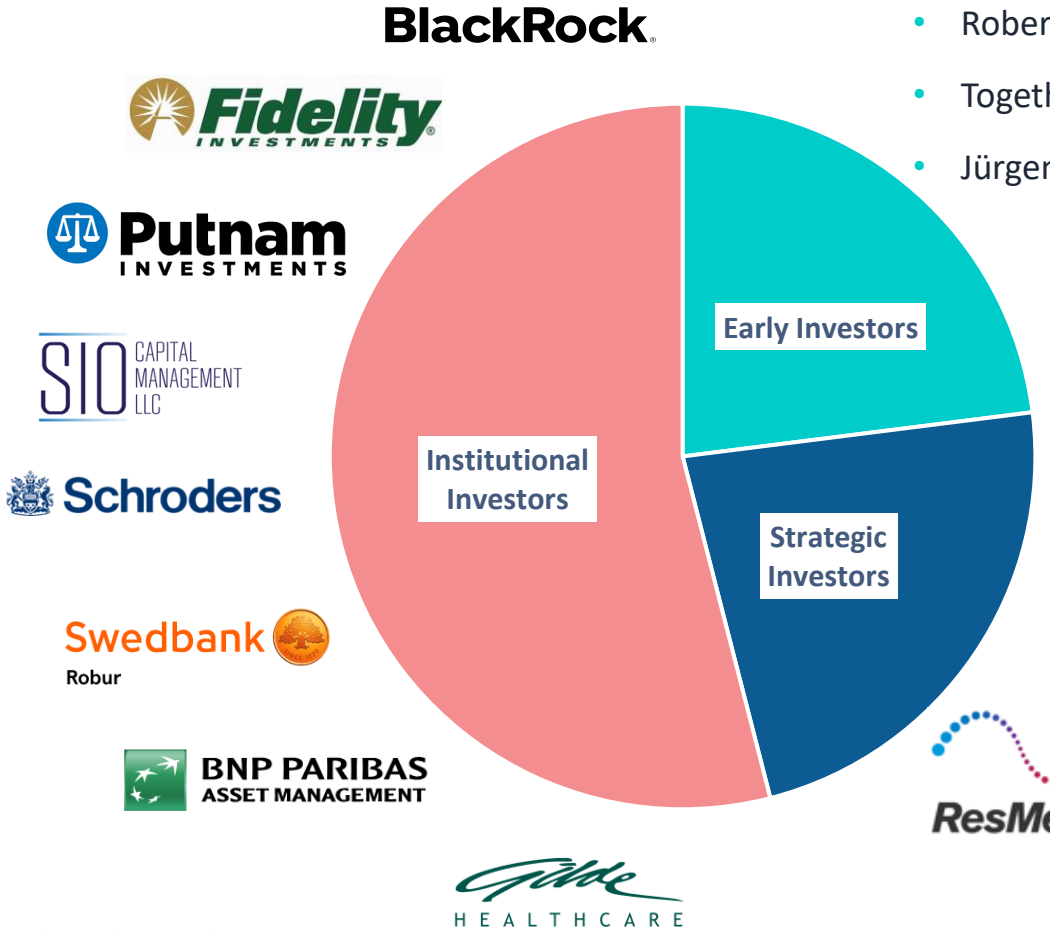
# Solid Investor Base Provides Cash Runway Into Second Half 2026

## Cash Runway into H2 2026




## Shareholders Base

Nasdaq EURONEXT




- Robert Taub
- Together Partnership
- Jürgen Hambrecht

* On July 3rd 2024, the European Investment Bank (EIB) granted Nyxoah a facility of up to €37.5m of which of €10m was drawn down in July 2024
** On October 7, 2024 Nyxoah raised $27M (€25M) in gross proceeds pursuant to the $50M at-the-market offering



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