

Nyxoah

May 2022

Nyxoah 

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Investment Highlights

Significant Underpenetrated Global OSA Market Opportunity

- 425m moderate-to-severe OSA patients globally eligible for treatment
- >1m OSA patients eligible for HGNS treatment annually in US and Europe
- HGNS treatment solution now fully accepted by physicians and payors

Innovative Patient-Centric Technology

- Minimally invasive single-incision procedure
- Bilateral stimulation with external power source and no lead tunneling
- Patient-centric scalable technology platform with full-body 3.0T MRI compatibility

Growing Body of Strong Clinical Data

- BETTER SLEEP first study to demonstrate efficacy in CCC patients (60% response rate)
- DREAM IDE pivotal trial to secure US regulatory approval in early 2024
- Ongoing EliSA study generating 5-year safety and efficacy data

Targeted Commercial Strategy

- Centers of Excellence development built on strong ENT and Sleep Physician partnerships
- Market leadership in Germany by end of 2022 represents commercial proof of concept
- US pre-commercial activities focused on payor coverage and physician relationships

Healthy Financial Position

- Dual-listed company trading on Nasdaq and EuroNext stock exchanges
- €128 million cash balance after two successful IPOs, which brought in top tier investors
- Ample liquidity to fund key R&D, clinical, and commercial priorities into 2024

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

CEO

- 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.



Loïc Moreau

CFO

- Experienced Finance leader
- 13 years in Pharmaceutical healthcare at GSK with roles in Corporate Development/ M&A (UK), Finance R&D (UK) or Country CFO where he notably led and structured the various support functions for GSK business in France (€1bn+ turnover)
- Started his career at EY (external audit) followed by PwC (Corporate Finance)
- Joined Nyxoah in 2022 to take the leadership of the finance department.

Experienced Management Team



Bruno Onkelinx
CTO

- Has 25 years of experience in highly regulated industries with the last 15 years at Cochlear.
- At Cochlear he built successful teams while managing international research & development and manufacturing operations across Europe-Belgium and the US-Colorado.



An Moonen
General Counsel

- Joined Nyxoah in December 2020 as General Counsel, bringing over 20 years of experience
- Was involved in various strategic licensing, financing and M&A transactions, including TiGenix' Nasdaq IPO



Jey Subbaroyan
VP Clinical Affairs

- Has 14 years of experience in clinical and pre-clinical neuromodulation research in the fields of urology, migraine, spinal cord injury...
- Has successfully executed multiple clinical studies across the US, Europe and Australia managing diverse global teams



Nathalie Gilat
VP RA – GM Israel

- Has over 14 years of experience in global clinical & regulatory affairs
- Joined Nyxoah in 2014 and played a key role in its initial clinical studies obtaining CE mark and achieving regulatory milestones in the US



Rémi Renard
VP Market Development & Education

- Has over 15 years of experience in Sales and Marketing
- Has held multiple sales and marketing positions in medical device firms, mostly in the Cardiac Rhythm Management and OSA fields at Resmed, Boston Scientific and St. Jude Medical



Dorit Nahari
VP QA

- Has 13 years of experience in process manufacturing and quality management in highly regulated industries
- Has successfully led both small and large groups in numerous manufacturing aspects including routine production, implementation of process changes, qualifications of new manufacturing sites and preparation to regulatory audits



Patrick Tompkins
VP US Operations

- Has over 20 years of executive leadership experience in the medical device space
- Has previous commercial leadership experience, both in the cardiac and neuro fields, the last 13 years with neuromodulation companies, including St. Jude Medical



Jeremy Feffer
VP Investor Relations & Corporate Communications

- Has 20 years of experience in healthcare capital markets as a sell-side equity research analyst and an investor relations advisor.
- As an IR Director at LifeSci Advisors, he developed and executed comprehensive capital markets, corporate access, and messaging strategies for pre-IPO and publicly-traded healthcare companies.

Nyxoah™

Large and Underpenetrated Global OSA and HGNS Market Opportunity

Worldwide Obstructive Sleep Apnea Prevalence

936 Million

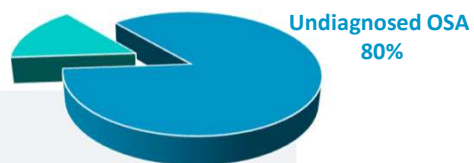
- 936M individuals (30-69 year) are estimated to suffer from OSA¹

425 Million

- 425M suffer from moderate to severe OSA, requiring therapy¹
- Increasing prevalence of OSA due to rise in obesity

20%

- Only 20% OSA patients are diagnosed²



Hypoglossal Nerve Stimulation Market Opportunity

>1 million eligible annually in key geographies

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

< 25,000 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

+70% CAGR HGNS revenue 2016 – 2021³

- 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 2022

A Disruptive Patient-Centric Solution TODAY...

Single incision procedure

Leadless and
battery-free

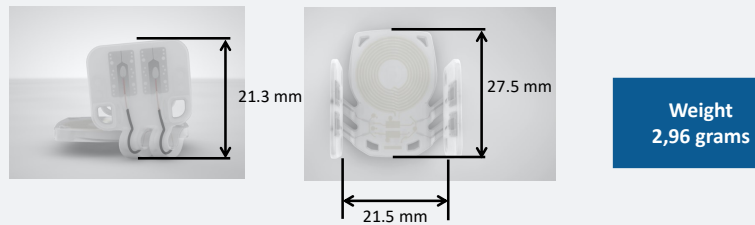
Full-body 1.5T and 3T MRI
compatible

Bilateral stimulation

CCC FDA breakthrough designation
CCC indication in Europe

Scalable platform

Genio® Implantable Stimulator



Genio® Activation Chip



Nyxoah™

Our Vision: Improving Lives Through Restful Nights

Connectivity & Remote Care

- Connectivity with remote smartphone application
- Cloud based access for patients and physicians



Patient Engagement

- Feedback to / from the patient for optimized compliance & comfort



Predictable Outcomes & Auto-Titration

- Patient acclimation through amplitude adjustment @ home
- Sensors for adaptive therapy & auto-titration



Nyxoaah™

The Genio® Duty Cycle Approach to Hypoglossal Nerve Stimulation

The Genio® proprietary Duty Cycle algorithm

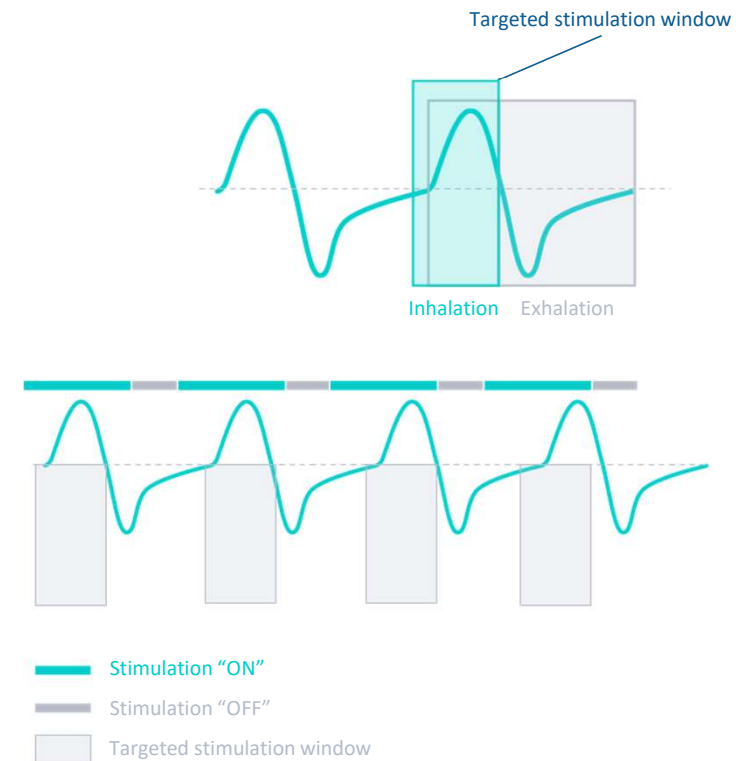
1 Respects the patient physiological breathing

- The patient breathing frequency is used as a reference to adjust the stimulation cycle

2 Ensures a timely and efficient stimulation, through Duty Cycle

- Genio® Duty Cycle algorithm: alternance of ON/OFF stimulation phases in a cyclical pattern
- The cyclical “ON” phase overlaps with the target window (end of expiration + early inspiration) to deliver a timely stimulation
- The “OFF” phase prevents the occurrence of nerve and muscle fatigue

Genio® algorithm example

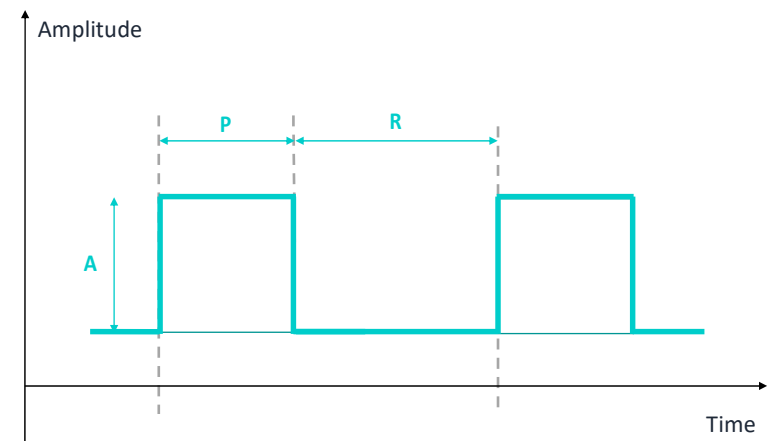


Stimulation Parameters for Optimal Therapy Efficiency

- Efficient therapy through patient customized parameters
- Optimal patient comfort:
 - Tolerable paraesthesia and no tingling sensation
 - Therapy activation once patient is asleep
 - Gradually ramping-up stimulation after therapy has started

Parameter	Description	Ranges
Pulse Amplitude (A)	Stimulation amplitude	1-100 %
Pulse Duration (P)	Duration of one stimulation pulse	50-250 μ sec
Pulse interval (R)	Interval between 2 pulses	--
Pulse Frequency ($1/(P+R)$)	Number of pulses per second	30-50 Hz

- Resulting in proven therapy compliance:
 - 91% patients using the Genio® system more than 5 days a week
 - 77% patients with a nightly use of more than 5 hours a night
- 82% patients satisfied with the Genio® system²¹



21. Eastwood PR, Barnes M, MacKay SG, et al. Bilateral Hypoglossal Nerve Stimulation for Treatment of Adult Obstructive Sleep Apnea. Eur Respir J 2019; <https://erj.ersjournals.com/lookup/doi/10.1183/13993003.01320-2019>

The Genio® System – Addressing Unmet Physician Needs

Physician

Single incision procedure

- Extended operative time is associated with increased risk of surgical site infection¹³

Leadless

- Up to 25% failure rate of percutaneous leads after 5Y¹⁴

External power-source

- Device replacement and revision procedures are associated with a two- to four-fold higher risk of infection¹⁵

Bilateral stimulation

- Genio® indicated for non-CCC and CCC patients
- No need for a DISE to exclude CCC at the soft palate level

Nyxoah®

Inspire
Sleep Apnea Innovation

LivaNova  **INTHERA**

Implantable parts	1 – Genio® IS	3 – Pulse generator + 2 leads	2 – Pulse generator + lead
Number of incisions	1 incision	2 incisions	2 incisions
Lead(s)	0 – No lead	2 – Stimulation and breathing	1 – Stimulation
Tunneling	No tunneling	At least 1 step	1 step
Power source	External	Implanted battery	Implanted battery
Estimated implantation time	1 hour	2.5 hours	2 hours

13. Cheng et al. Prolonged Operative Duration Increases Risk of Surgical Site Infections: A Systematic Review. Surg Infect (Larchmt). 2017 Aug 1; 18(6): 722–735

14. Schultz et al. Neuromodulation. SCS —The Implantable Systems Performance Registry (ISPR) 2016 Dec; 19(8): 857–863

15. Döring et al. The Diagnosis and Treatment of Pacemaker-Associated Infection. Dtsch Arztebl Int. 2018 Jun; 115(26): 445–452

The Genio® System – Addressing Unmet Patient Needs

Patient

User-centric

- No bulky pulse generator under the skin / Only one discreet scar in the chin fold

Indicated for CCC and non-CCC patients

- CCC prevalence is up to 35% in OSA patients

External power-source & Chip

- No need for surgical reintervention due to battery depletion
- Simple and straight forward upgrades through external chip

MRI compatibility

- >40 Million MRI scans performed in 2020 in OSA patients¹⁷
- 60% MRI scans are performed in the thorax/abdominal area¹⁷
- 40% MRI scans are 3T¹⁷

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Inspire
Sleep Apnea Innovation

LivaNova  INTHERA

Number of scars	1 – in the chin fold	At least 2 scars	2 scars
Power source	External	Implantable Pulse Gen	Implantable Pulse Gen
Stimulation	Bilateral	Unilateral	Unilateral
MR conditional labelling	Full-body 1.5T and 3T	Extremities only 1.5T only	No

17. Magnetic Resonance Imaging MARKET ESTIMATES & TREND ANALYSIS - Grand View Research Market data 2021

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2021 Key Achievements – Focused on Execution

Jan

- MR Conditional Labeling – 1.5T & 3T / Full-Body

Feb

- VANDERBILT University Exclusive Licensing (Ansa Cervicalis)

May

- BETTER SLEEP Study Achieves 6-Month Safety and Performance Endpoints

June

- Germany Commercial Proof of Concept – DRG / 12 active accounts
- First revenue in Spain, Belgium + Swiss DRG

July

- NASDAQ IPO – \$97.8M raised

Sept.

- Breakthrough designation for OSA CCC patients

Oct.

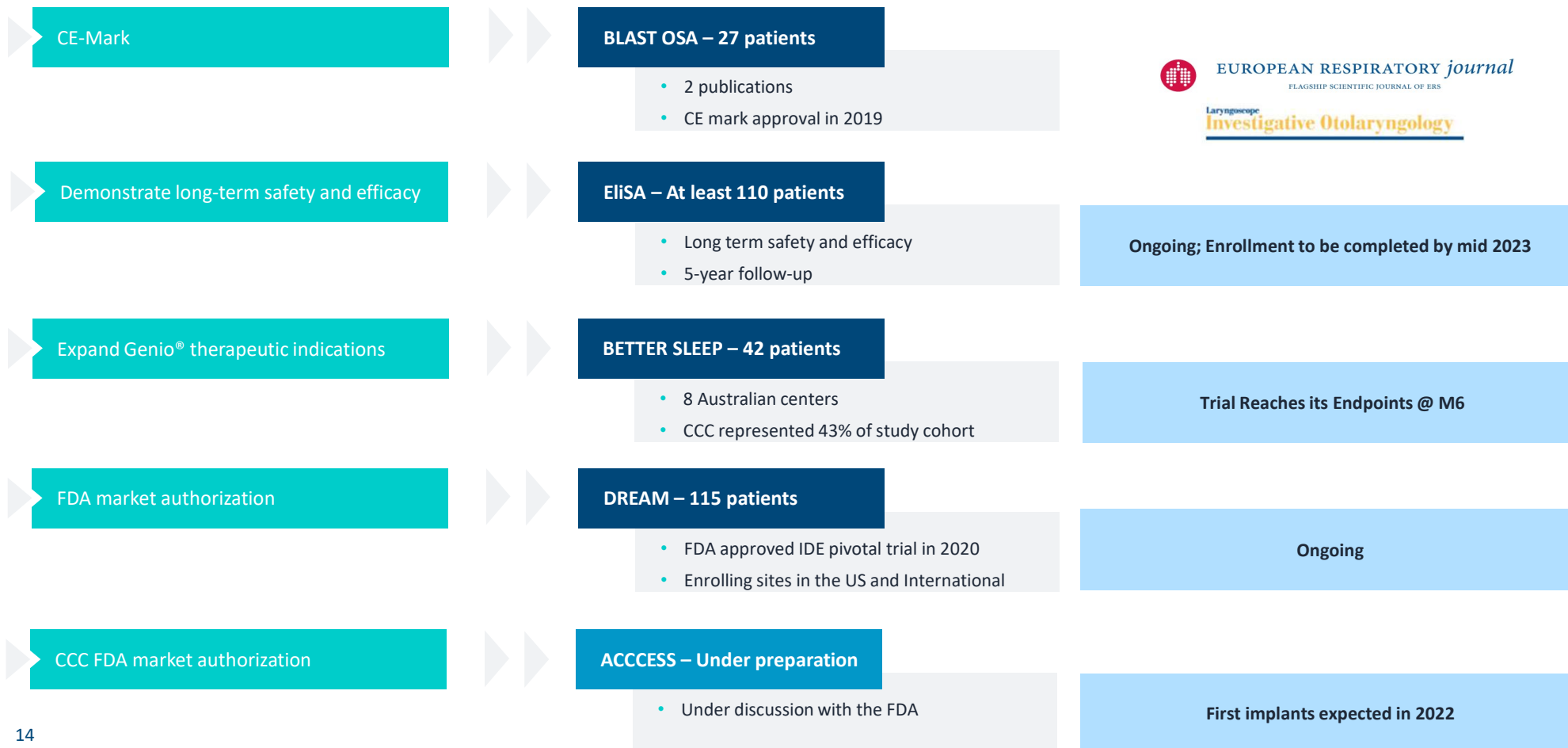
- CE-Mark indication approval to treat CCC Patients

Dec.

- ACCESS study FDA sprint submission

Clinical Strategy

Building Robust Clinical Evidence



BETTER SLEEP

Study Design & Endpoints

Study Design

- Multicenter, prospective, open-label, two group study
- Safety and performance of bilateral HGNS system in adult patients evaluated
- With and without complete concentric collapse (CCC)

Major Inclusion & Exclusion Criteria

- Moderate-to-severe OSA
- Body mass index $\leq 32 \text{ kg/m}^2$
- Failed, refused or did not tolerate positive airway pressure therapy

Study Endpoints

Safety

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

Efficacy

- Primary – Mean reduction in AHI (4% oxygen desaturation, $\text{AHI}_{4\%}$) for the entire cohort*
- Exploratory – Mean reduction in AHI4 for the CCC subgroup*
- Secondary – Mean reduction in oxygen desaturation index scored at 4% desaturation ($\text{ODI}_{4\%}$) for the entire cohort*

*All assessments from consent (safety) or baseline (efficacy) to 6 months post-implant

15 Source: Lewis R. et al. Bilateral Hypoglossal Nerve Stimulation Improves Moderate to Severe Obstructive Sleep Apnoea in Participants With and Without Complete Concentric Collapse (BETTER SLEEP) – World Sleep Congress 2022 Abstract

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BETTER SLEEP

Demographics & Safety Results

Demographics

Screened	184 participants across 8 Australian sites
Implanted	42 participants
Demographics	74% were male
Age range	37-73 years
Mean BMI	28.5 ± 2.4 kg/m ²
CCC	18 participants (78% male, age range: 38-73 years, mean BMI 28.6±2.5 kg/m ²)

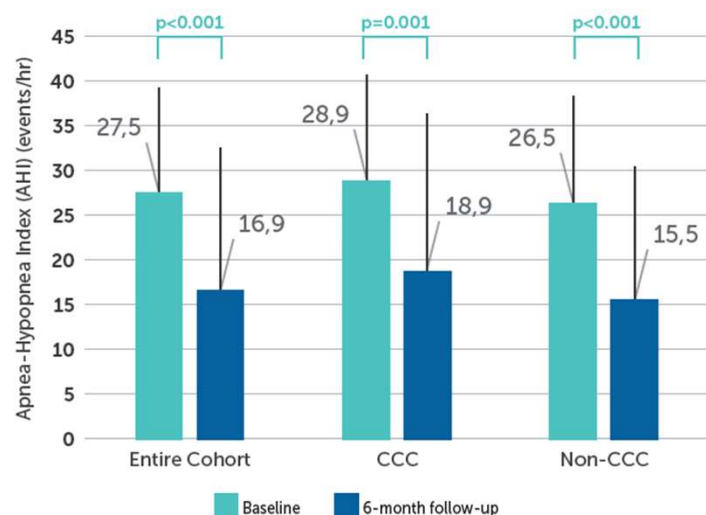
Safety

- Independent Clinical Events Committee: 3 device and/or procedure related SAEs in 2 subjects
 - Infection leading to explant
 - Device migration leading to replacement
 - Mild cellulitis secondary to folliculitis
- All SAEs resolved without sequelae

BETTER SLEEP

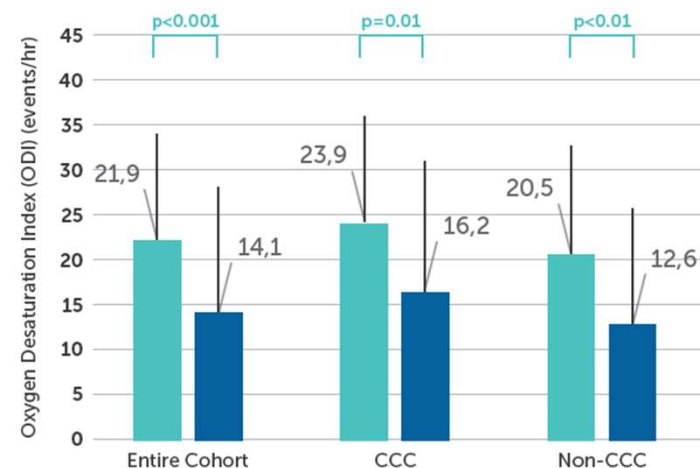
Efficacy Endpoints

Apnea Hypopnea Index – 4%



		Entire Cohort – n=42	CCC – n=18	Non-CCC –n=24
Baseline	Mean ± SD	27.54 ± 11.91	28.93 ± 11.86	26.49 ± 12.10
Month 6	Mean ± SD	16.89 ± 16.00	18.86 ± 17.59	15.51 ± 15.00
Delta	Mean ± SD	-10.65 ± 11.57	-10.07 ± 12.25	-10.98 ± 11.28
	p-value	<0.001	0.001	<0.001

Oxygen Desaturation Index – 4%



- Statistically significant reduction in AHI and ODI across all cohorts
- Similar improvements in AHI_{4%} and ODI_{4%} for both CCC and non-CCC participants (not powered)

BETTER SLEEP

Responder Rate – Sher Criteria

- 36 patients completed polysomnography at month 6
- Responder defined according to the Sher criteria²² ($\geq 50\%$ reduction in AHI and AHI less than 20)
- Strong responder rates help de-risk DREAM U.S. IDE study

	AHI _{4%} Responder Rate – Sher Criteria –
CCC & Non-CCC – n=36	64%
CCC – n=15	60%
Non-CCC – n=21	67%

Results subject to final review and validation

BETTER SLEEP

Improvement in $AHI_{4\%}$ in Responders

- >70% reduction in $AHI_{4\%}$ in responders in both CCC and non-CCC population
- Presence of “Super Responders” in both CCC and non-CCC cohorts provides additional validation

AHI responders	– $AHI_{4\%}$ – Mean % reduction at 6 months
Entire cohort	73.4%
CCC cohort	71.1%
Non-CCC cohort	74.9%

BETTER SLEEP – Data from the entire cohort

BETTER SLEEP

Key Takeaways

BETTER SLEEP study reached all efficacy endpoints

Statistically significant AHI_{4%} and ODI_{4%} reduction in:

- Full cohort
- CCC cohort
- Non-CCC cohort

Similar improvements in AHI_{4%} and ODI_{4%} for both CCC and non-CCC participants

Europe

- CCC patients are indicated for the Genio® therapy in Europe
- CE-Mark Instructions for use: *"The Genio® system is indicated to treat patients suffering from moderate to severe OSA with and without Complete Concentric Collapse (CCC) at the soft palate level"*
- No DISE required to assess presence of CCC at the soft palate level

United States

- Genio® received "Breakthrough Device Designation" in the US for CCC patients
- Ongoing discussions with FDA to initiate ACCESS IDE study in 2022

DREAM Study – IDE Pivotal Trial

Population and key inclusion criteria

22 < Age < 75

Failed, did not tolerate or refused PAP

Combined central/mixed AHI > 25% total AHI excluded

BMI ≤ 32 kg/m²

Moderate to severe OSA – AHI 15-65

CCC of soft palate excluded

Target: 134 patients implanted

Safety and Performance

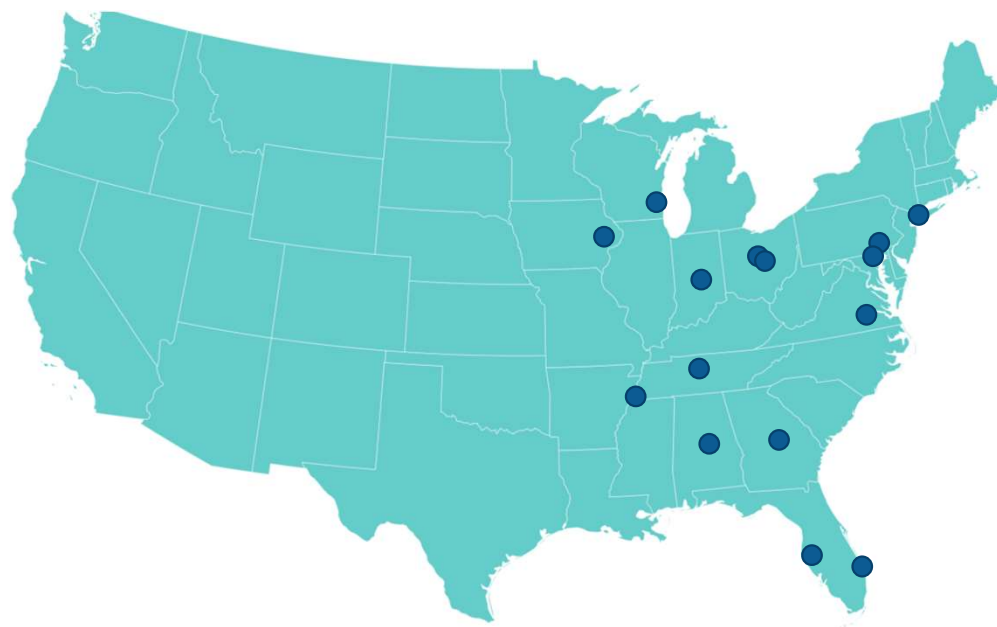
- Safety: Incidence of device-related serious adverse events at 12 months
- Co-primary effectiveness endpoints: Percentage of responders at 12 months based on Apnea Hypopnea Index (AHI4%) using the Sher criteria and percentage of responders at 12 months based on ODI4% (25% reduction of ODI between baseline and 12-month visit)

Status

- FDA approved IDE pivotal trial in June 2020 – Up to 25 participating sites
- 18 US sites activated, screening, enrolling and implanting patients
- 7 International sites activated, screening, enrolling and implanting patients
- Mix of large academic centers & private practices, all HGNS experienced

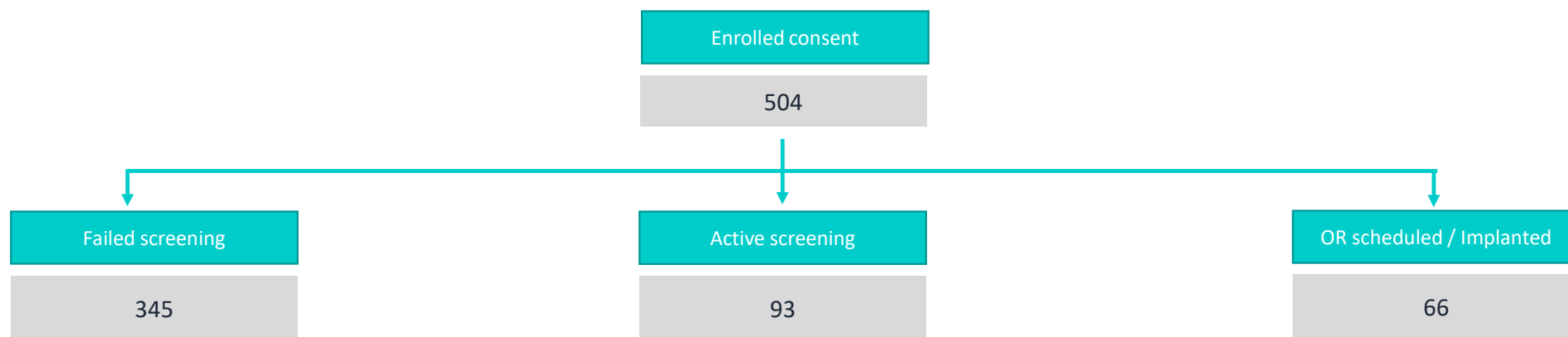
DREAM Study – US Active Sites

Principal Investigator	Institution & Location
Kirk P. Withrow MD	UAB, Birmingham, AL
Samuel Mickelson MD, FACS	Advanced ENT, Atlanta, GA
Colin Huntley MD & Maurits S. Boon MD	Thomas Jefferson Philadelphia, PA
Tapan A. Padhya MD	USF, Tampa General MC, Tampa, FL
Marion Boyd Gillespie MD	UT, Memphis, TN
Melyssa K. Hancock MD	ENT & AAF, Boca Raton, FL
Tod C. Huntley MD	CENTA, Carmel, IN
Raj C. Dedhia MD, MSCR	Penn, Philadelphia, PA
Maria Suurna MD	Cornell, Manhattan, NY
Doug Van Daele MD	Univ Iowa, Iowa City, IA
B. Tucker Woodson MD	MCW, Milwaukee, WI
David Kent MD	VUMC, Nashville, TN
Asim Roy MD	OSMI, Dublin, OH
Ulysses Magalang MD	OSU, Columbus, OH
Ryan Nord MD	VCU, Richmond VA



United States

DREAM Study – Status Update (Week of 2 May 2022)



- Status
 - Patient drop out (~60%) from Enrolled to Implant driven by DISE, PSG, BMI
- US commercialization expected Q1 2024
 - 12 months data on full study cohort (134 patients)
 - Regulatory path clarity (De Novo vs. PMA) based on 6 months safety data

Commercial Leadership Through Focused Execution

Go Deep versus Go Wide



EU Market Access

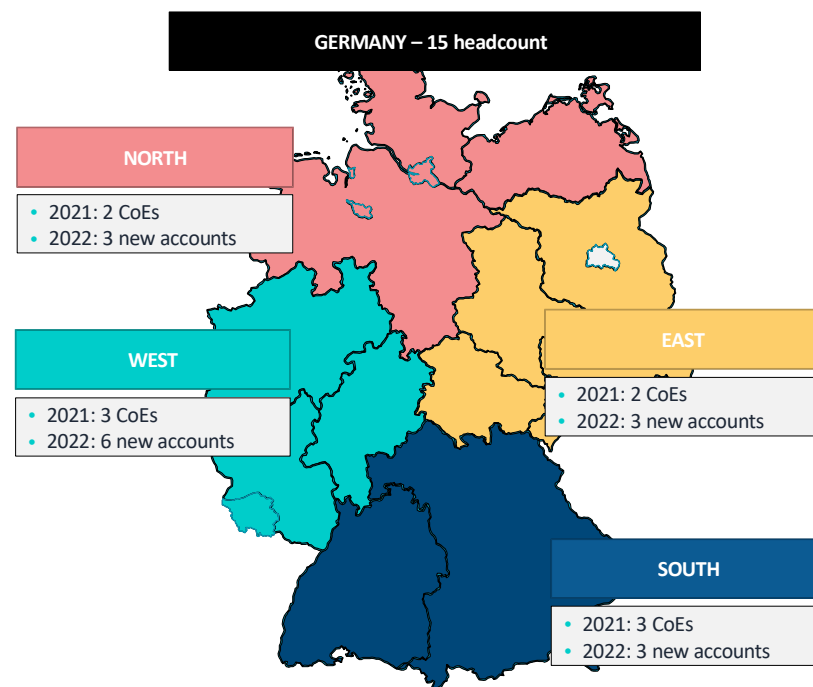
Nyxoah – EU reimbursed countries

- Germany – 2021: Dedicated DRG code
- Switzerland – 2021: Dedicated DRG code
- Spain – 2021: Funding through hospital budget

Nyxoah – EU expected reimbursement

- The Netherlands
- Belgium
- Nordics

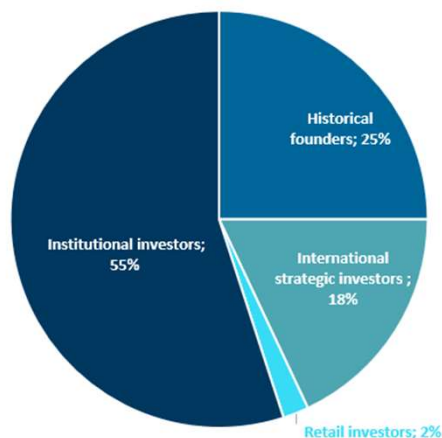
Germany - Proof of concept



High Quality and Diverse International Shareholder Base

Euronext IPO EURONEXT

- September 2020
- Base offering & over-allotment: €85M (\$100M)



Nasdaq IPO

- July 2021
- Base offering & over-allotment: \$97.8M

Current Shareholder Base (as of 12/31/21)

Historical Shareholders

- Robert Taub
- Together Partnership
- Jürgen Hambrecht

International strategics



US Institutional

BlackRock.

DEERFIELD
Advancing Healthcare®



RTW
Investments

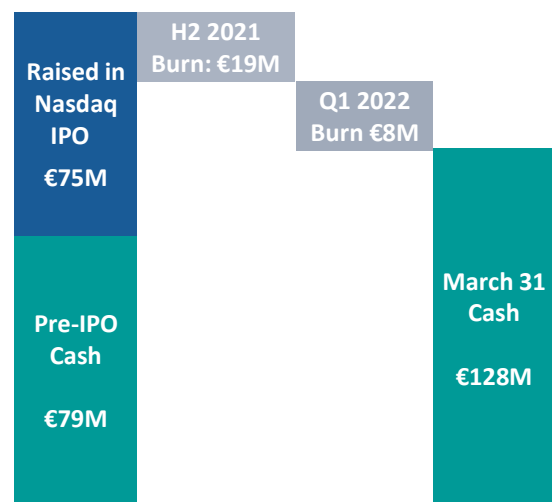


EU Institutional

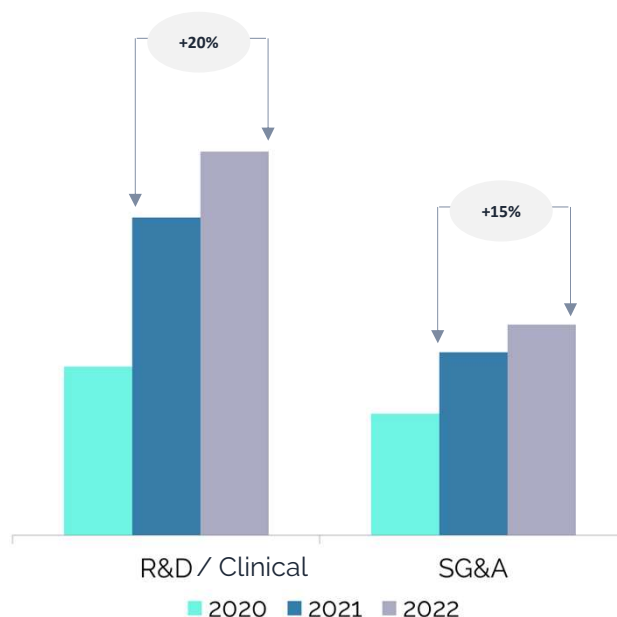


Strong Cash Position Supports Clinical and Commercial Priorities in 2022 and Beyond

Strong Cash Position - €128M



Operating Expense Growth (in €)



- Operating expenses to increase by ~19% in 2022
- R&D/Clinical to represent ~45% of 2022 expenses driven by DREAM enrollment completion, ELISA study progress, and ACCESS study commencement
- SG&A drivers include increased commercial efforts in Germany to achieve market leadership and scale-up of corporate functions

Thank you

Q&A

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