trevi® THERAPEUTICS

Controlling cough where it counts™

# Corporate Presentation

June 2026

Nasdaq: TRVI

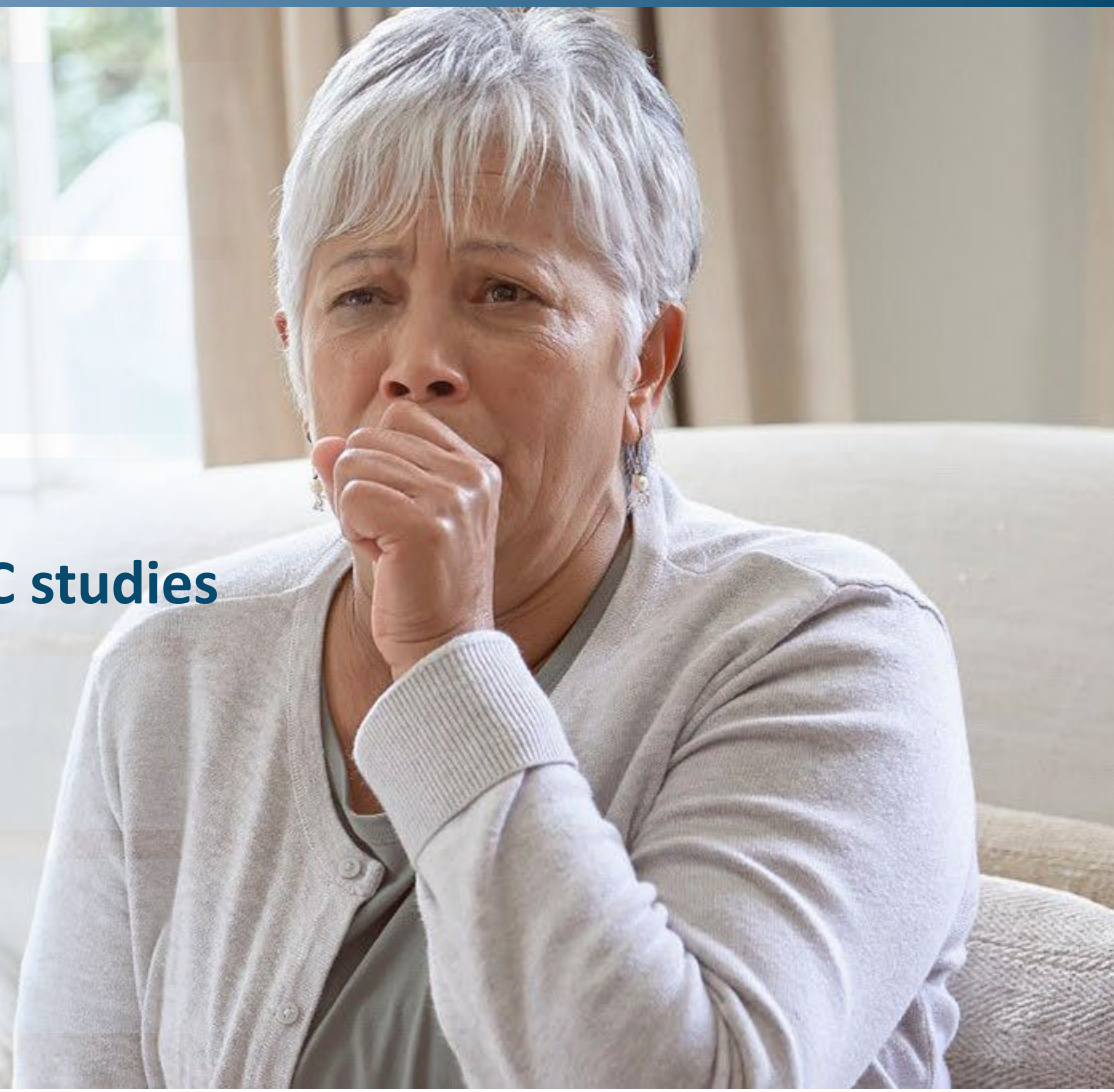
# Forward Looking Statement Disclaimer

Statements contained in this presentation and oral statements made regarding the subject of this presentation regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements are subject to risks and uncertainties and actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding Trevi's business plans and objectives, including future plans or expectations for Haduvio (nalbuphine ER) and plans with respect to clinical trials, expectations regarding Trevi's uses and sufficiency of capital, and other statements containing the words "believes," "anticipates," "plans," "expects," and similar expressions. Risks that contribute to the uncertain nature of the forward-looking statements include: uncertainties regarding the success, cost and timing of Trevi's product candidate development activities, and ongoing and planned clinical trials; the risk that positive data from a clinical trial may not necessarily be predictive of the results of future clinical trials in the same or a different indication; uncertainties regarding the commercial potential of Haduvio and Trevi's ability to execute on its strategy; uncertainties with respect to regulatory authorities' views as to the data from Trevi's clinical trials and next steps in the development path for Trevi's Haduvio in the United States and foreign countries; uncertainties inherent in estimating Trevi's cash runway, as well as other risks and uncertainties set forth in the quarterly report on Form 10-Q for the quarter ended March 31, 2026 filed with the Securities and Exchange Commission and in subsequent filings with the Securities and Exchange Commission. All forward-looking statements contained in this presentation speak only as of the date on which they were made. Trevi undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

This presentation includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We believe that these third-party sources and estimates are reliable but have not independently verified them. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors that could cause results to differ materially from those expressed in the estimates made by third parties and by us.

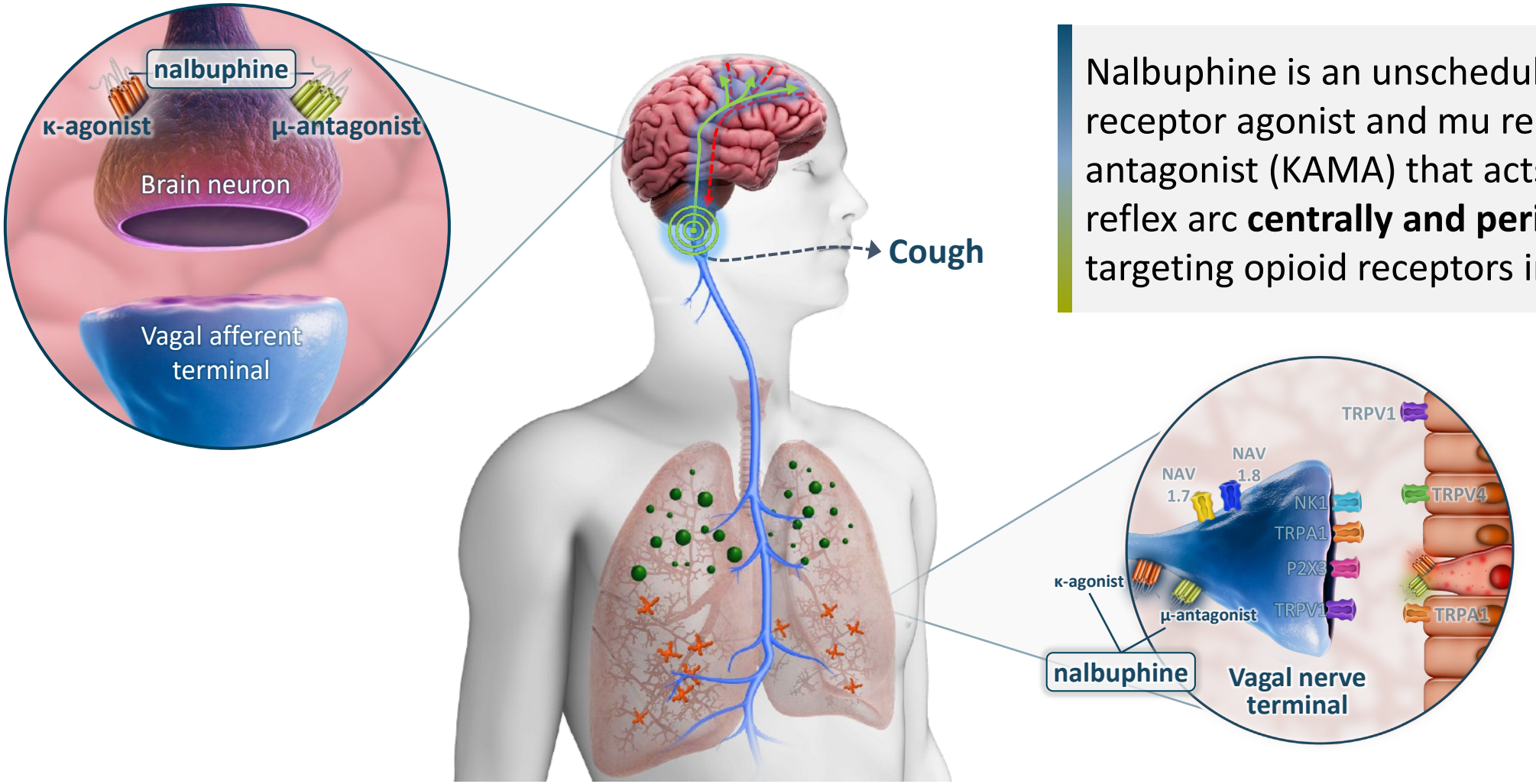
# Best-in-Class Potential for Haduvio (nalbuphine ER) Across Difficult to Treat Chronic Cough Conditions

- Significant unmet need*
- Differentiated central and peripheral mechanism
- Only investigational therapy with positive results in IPF-related chronic cough and RCC studies
- Potential for specialty pricing and sales model
- $6B+ peak sales opportunity



IPF: Idiopathic Pulmonary Fibrosis, RCC: Refractory Chronic Cough
*No approved therapies in the US for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

# Nalbuphine ER Has a Differentiated Central and Peripheral Mechanism of Action




Nalbuphine is an unscheduled kappa receptor agonist and mu receptor antagonist (KAMA) that acts on the cough reflex arc **centrally and peripherally** by targeting opioid receptors involved in cough

κ-agonist, kappa opioid receptor agonist; μ-antagonist, mu opioid receptor antagonist; ER, extended release; NAV 1.7, voltage-gated sodium channel, subtype 1.7; NAV 1.8, voltage-gated sodium channel, subtype 1.8; NK1, neurokinin 1 receptor; NMDA, N-methyl-D-aspartate receptor; P2X3, P2X purinoceptor 3; Pannexin 1, pannexin-1 channel; TRPA1, transient receptor potential ankyrin 1; TRPV1, transient receptor potential vanilloid 1; TRPV4, transient receptor potential vanilloid 4.

1. Chung KF et al. *Nat Rev Dis Primers*. 2022;8(1):45. 2. Krajnik M et al. *Curr Opin Support Palliat Care*. 2014;8(3)191-199. 3. Birring SS et al. *Lung.* 2025;203(1):1-8.

Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

# Opioid Class Differences and Abuse Liability Are Explained by Receptor-Level Interactions – *Nalbuphine was Designed to be Unique*

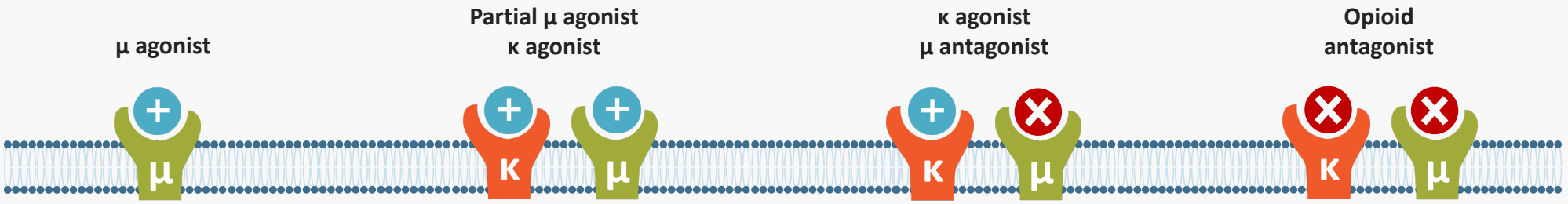
## Differences in opioid receptor interactions across medication classes drive variation in therapeutic and safety outcomes

**Opioid receptors**

κ-opioid receptor | μ-opioid receptor | δ-opioid receptor | NOP receptor

- **Nalbuphine is in a unique** opioid class called "mixed agonist-antagonist"
- This **kappa agonist/mu antagonist** class **was designed** to mitigate abuse potential and **minimize risks of respiratory depression, euphoria, and abuse**
- Parenteral nalbuphine (approved 1979) for moderate-to-severe pain, including during labor and delivery, is currently not controlled in the United States, reflecting the **low abuse potential**

**Class of medication**




**Examples**

| μ agonist | Partial μ agonist / κ agonist | κ agonist / μ antagonist | Opioid antagonist |
|---|---|---|---|
| Fentanyl, morphine, hydromorphone, oxycodone, codeine, hydrocodone | Butorphanol Pentazocine | **Nalbuphine** | Naloxone, naltrexone |
| Schedule II | Schedule IV | **Not scheduled** | **Not scheduled** |
| **Higher abuse potential** | | | **Lower abuse potential** |

Schedule II/IV refers to the US Controlled Substances Act scheduling.
κ, kappa opioid receptor; μ, mu opioid receptor, NOP, nociception/orphanin FQ.

1. Gabay M. *Hosp Pharm*. 2013;48(8):644-645. 2. Yaksh TL, Wallace MS. In: Hilal-Dandan R, Brunton LL. eds. Goodman and Gilman's Manual of Pharmacology and Therapeutics, 2nd ed. McGraw-Hill Education; 2016.

# Idiopathic Pulmonary Fibrosis (IPF)-Related Chronic Cough and non-IPF Interstitial Lung Disease (non-IPF ILD)-Related Chronic Cough

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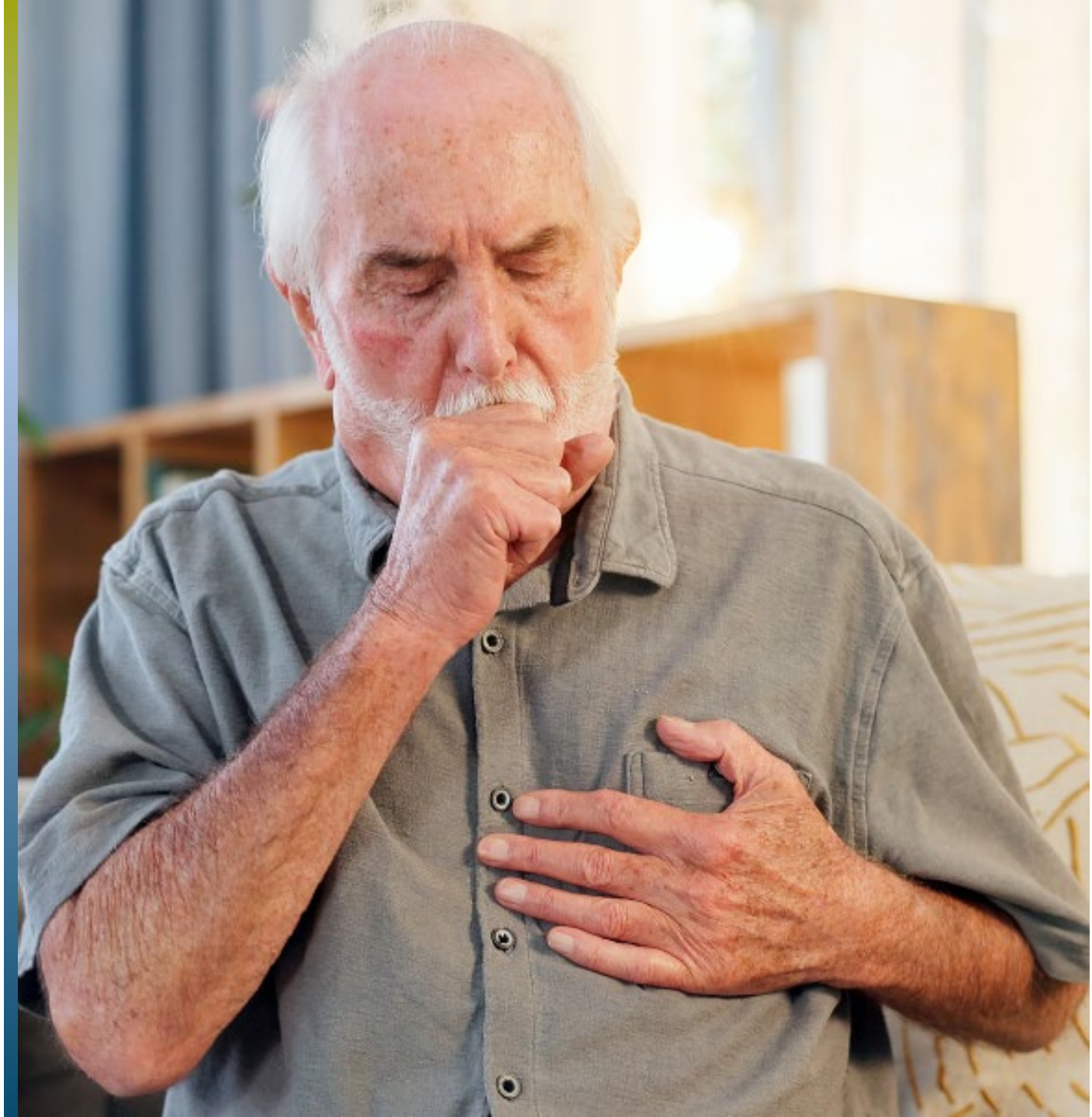
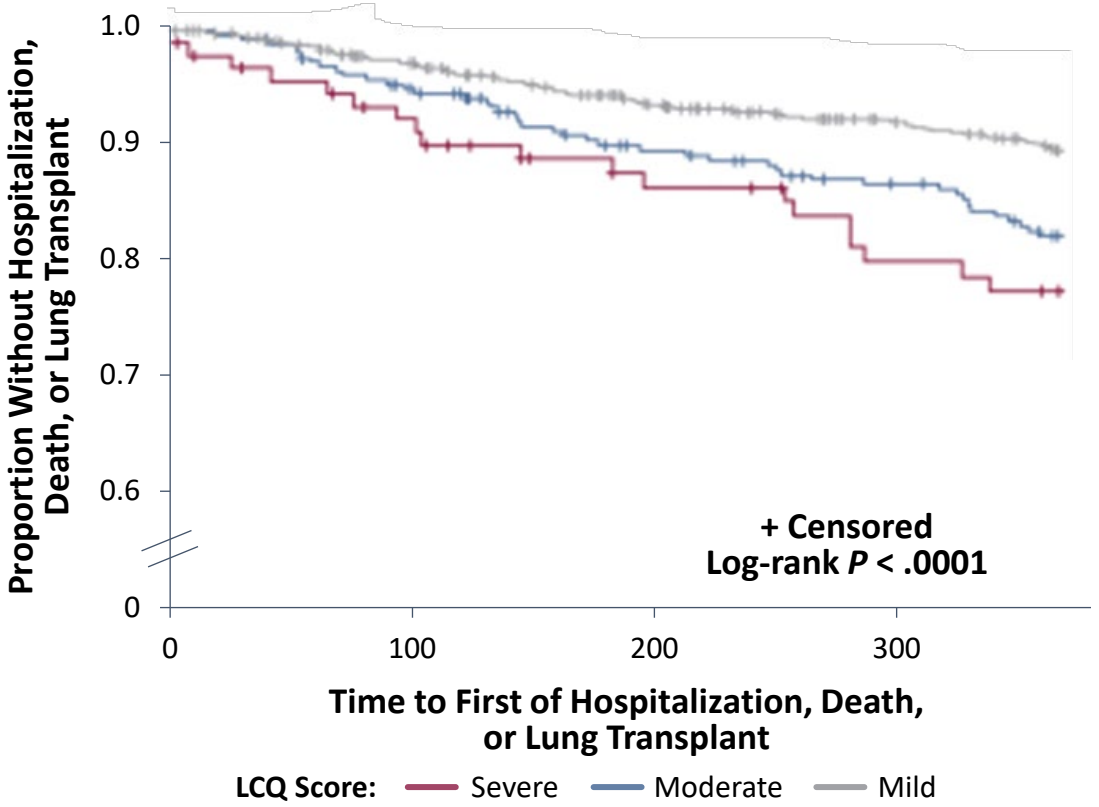


# Chronic Cough in ILDs May Cause Damage to the Lungs and Deteriorates Quality of Life

- No FDA-approved therapies for IPF-related or non-IPF ILD-related chronic cough
- Growing category of 140k US patients with IPF[1-3]
- 60-70% of IPF patients have uncontrolled chronic cough[4]
- 3-5 year life expectancy for IPF patients[5]
- Cough's role in IPF/ILDs[6-9]:
  - Worse cough QoL is associated with an increased risk of health outcomes (i.e. respiratory hospitalization, death)*
  - Pro-fibrotic
  - Can cause fatigue, air hunger, and peripheral oxygen desaturation

## Estimates for Respiratory Hospitalization, Death, and Lung Transplant by LCQ Score (Cough QoL) Severity Over Time for ILD Patients from the US Pulmonary Fibrosis Foundation Registry (N=1,447)

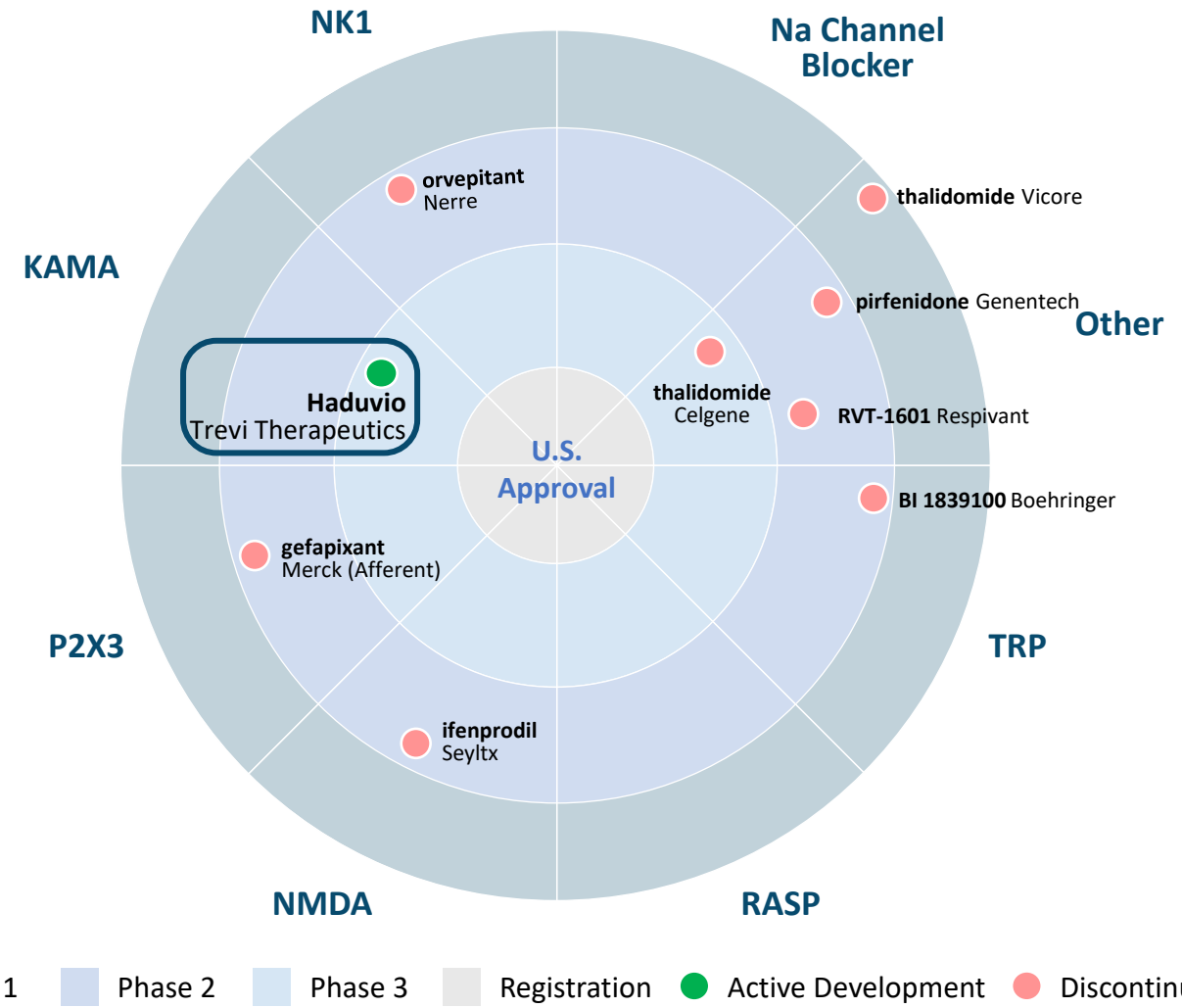



[1]Raghu G et al. ERJ 2016 doi: 10.1183/13993003.01653-2015 [2]Raghu G et al. Lancet Respir Med 2014 doi: 10.1016/S2213-2600(14)70101-8 [3]U.S. Census NC-EST2023-AGESEX-RES [4]Ryerson CJ et al. *Resp* 2011 doi: 10.1111/j.1440-1843.2011.01996.x [5]Raghu G et al. Lancet 2014 doi: 10.1016/S2213-2600(14)70101-8 [6]Lee J et al. CHEST 2022 doi: 10.1016/j.chest.2022.03.025 [7]Khor YH et al. AJRCCM 2024 doi: 10.1164/rccm.202311-2101OC [8]Mann J et al. Front Rehabil Sci 2021 doi: 10.3389/fresc.2021.751798 [9]Wakwaya Y et al. CHEST 2021 doi: 10.1016/j.chest.2021.05.071

Modified from Figure 2D in Lee J et al. *Chest*. 2022 Sep;162(3):603-613. DOI: 10.1016/j.chest.2022.03.025. QoL: Quality of Life

*Assessed via the Leichester Cough Questionnaire (LCQ)

# Opportunity to be Best-in-Class and First-in-Class in IPF-Related Chronic Cough




## Peripheral Mechanisms Have Failed in IPF-Related Chronic Cough

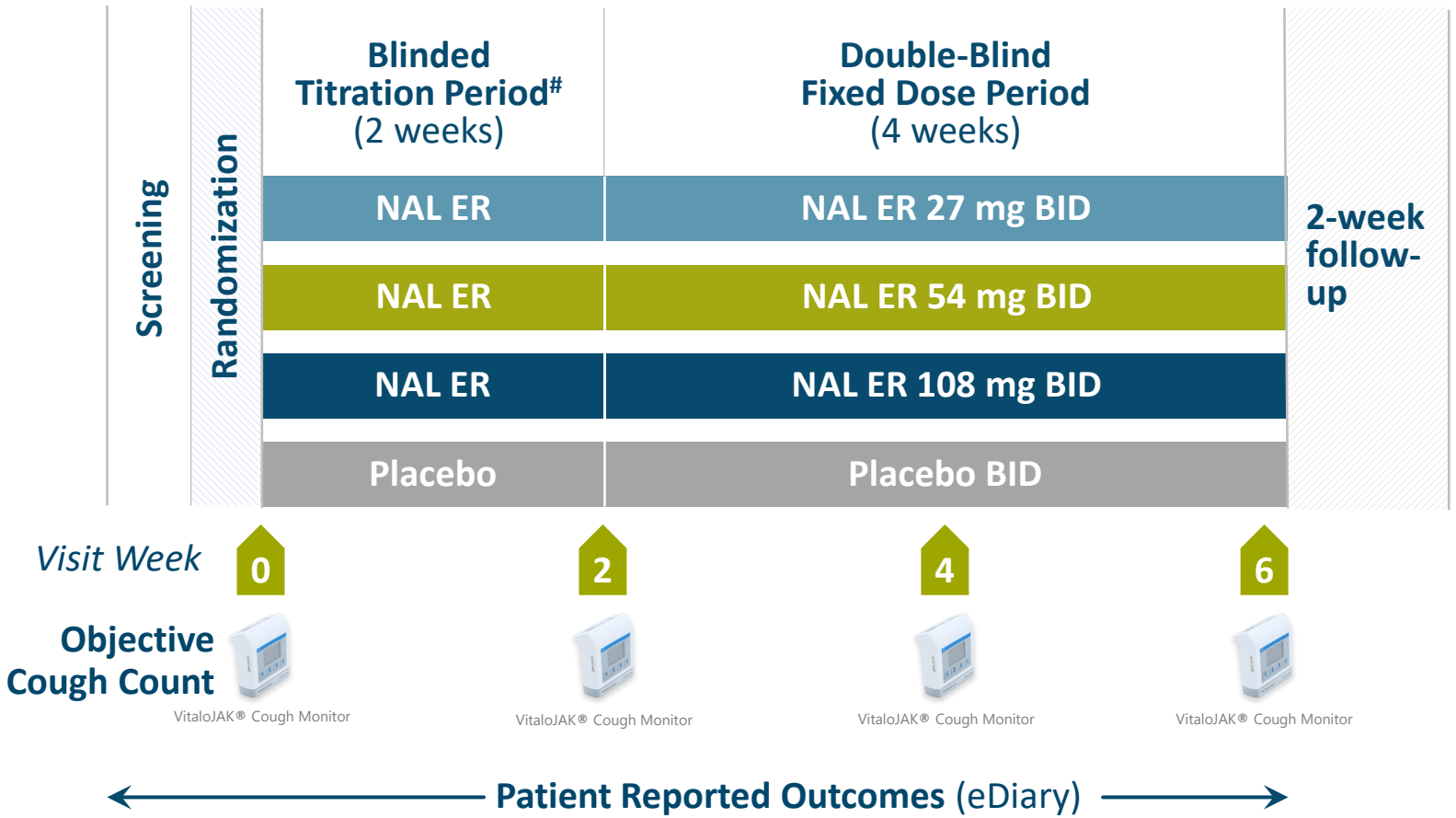
## Anti-Fibrotics Have Not Shown Cough Benefit

- Aim to slow the progression of the disease
- No statistically significant cough benefit

Sources: Haduvio, Trevi Therapeutics: DOI: 10.1056/EVIDoa2300083, Orvepitant, Nerre: clinicaltrials.gov/study/NCT05185089, Gefapixant, Merck: doi: 10.1007/s41030-021-00162-9, Ifenprodil, Seyltx: Algernon Pharmaceuticals Press Release January 9, 2023, Ifenprodil, Seyltx: Algernon Pharmaceuticals Press Release March 27, 2024, Thalidomide, Celgene: doi: 10.7326/0003-4819-157-6-201209180-00003, Thalidomide, Vicore: Vicore Press Release January 2, 2024., Pirfenidone, Genentech: doi: 10.1183/13993003.01157-2017, RVT-1601, Respivant: doi: 10.1164/rccm.202106-1485OC, RVT-1601, Roivant Sciences: doi: 10.1016/S2213-2600(17)30310-7, BI 1839100, Boehringer Ingelheim: clinicaltrials.gov/study/NCT06360094, Nintedanib: doi.org/10.1183/13993003.congress-2016.PA785

Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

# Phase 2b Clinical Trial Design in Patients with IPF-Related Chronic Cough (N=165)




## Primary Efficacy Endpoint

- Relative change from Baseline in 24-hour cough frequency versus placebo at Week 6 (using objective cough monitoring) *

## Secondary Efficacy Endpoints

- E-RS®:IPF Cough Subscale *
- CS-NRS *
- 24-hour cough frequency responder analysis (using objective cough monitor) *
- EXACT:IPF, LCQ, L-IPF, EQ-5D-5L
- PGI-S & PGI-C Cough, PGI-S & PGI-C IPF
- CGI-C, CGI-S

# Blinded titration period consisted of:
Day 1 - 2: 27mg QD
Day 3 - 7: 27 mg BID
Day 8 - 14: 54 mg BID (ONLY 54 mg BID and 108 mg BID dose groups)

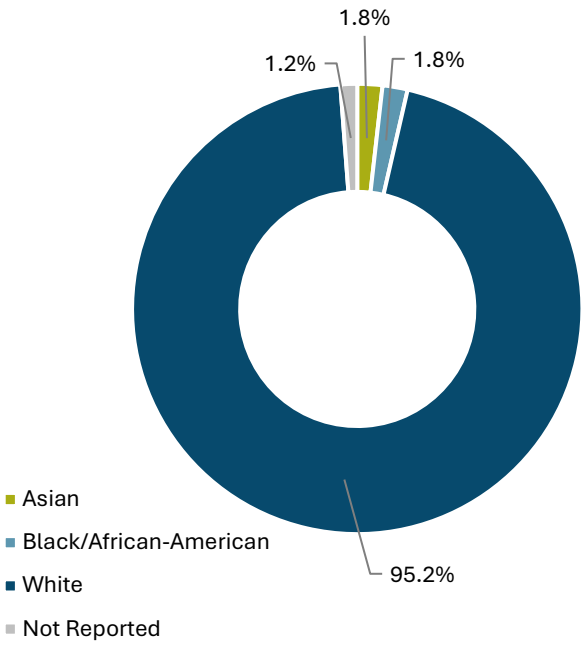
* Included in topline results

Haduvio (nalbuphine ER/NAL ER) is an investigational therapy

EXACT:IPF: Exacerbation of Chronic Pulmonary Disease Tool IPF, CS-NRS: Cough Severity Numerical Rating Scale, LCQ: Leicester cough questionnaire, L-IPF: Living with IPF, EQ-5D-5L: EuroQoL 5-Dimension 5-Level, PGI-S Cough: patient global impression of cough severity, PGI-C Cough: patient global impression of change in cough, PGI-S IPF: patient global impression of IPF symptom severity, PGI-C IPF: patient global impression of change in IPF symptoms, CGI-S: clinician global impression of cough severity, CGI-C: clinician global impression of change of cough

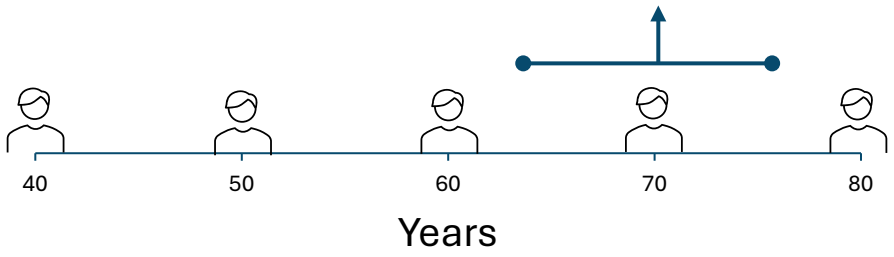
# Baseline Characteristics of 165 Randomized Patients

## Race



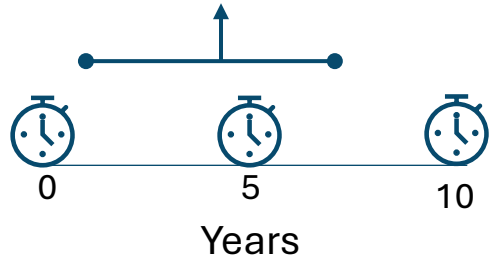

## Age

**Mean (SD): 70.1 (7.3) years**

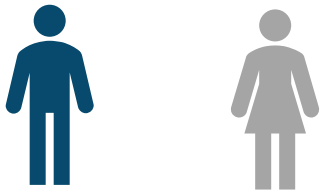



## Duration of Cough

**Mean (SD): 4.2 (6.6) years**




## Sex



**Male** **71.5%**

**Female** **28.5%**

## Lung Function Parameters

**Mean (SD) $FEV_1$ liters: 2.6 (0.9)**

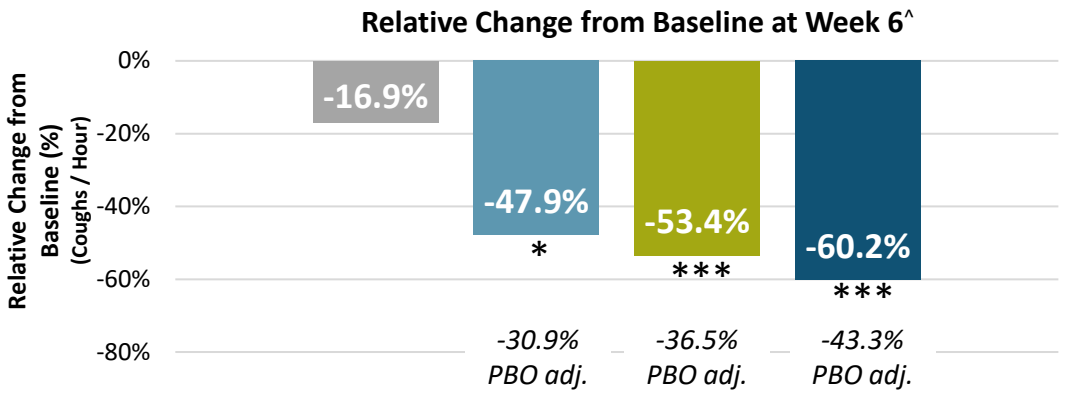
## Cough Frequency

**Mean Dose Group Range:**
**24.6 – 31.5** (coughs/hour)
**590 – 750** (coughs/day)

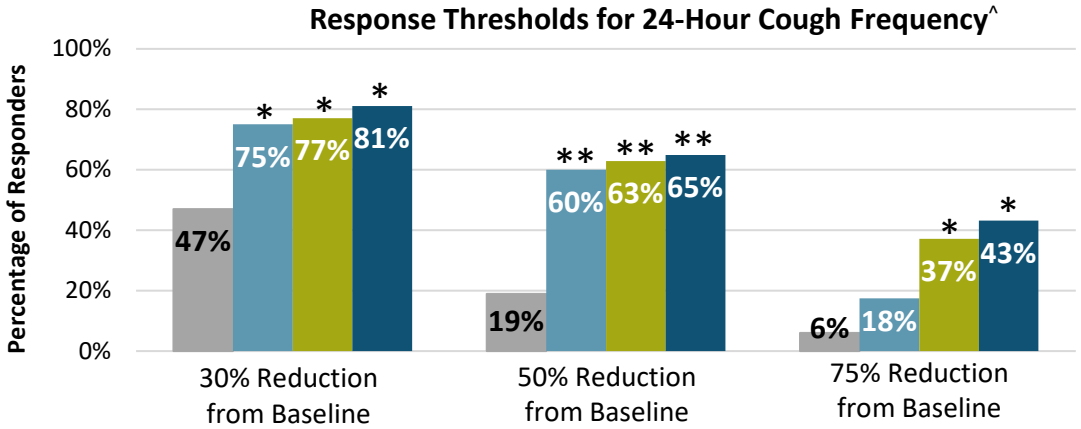
FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation.

# Rapid, Persistent, and Broad Response Observed in CORAL Phase 2b Trial

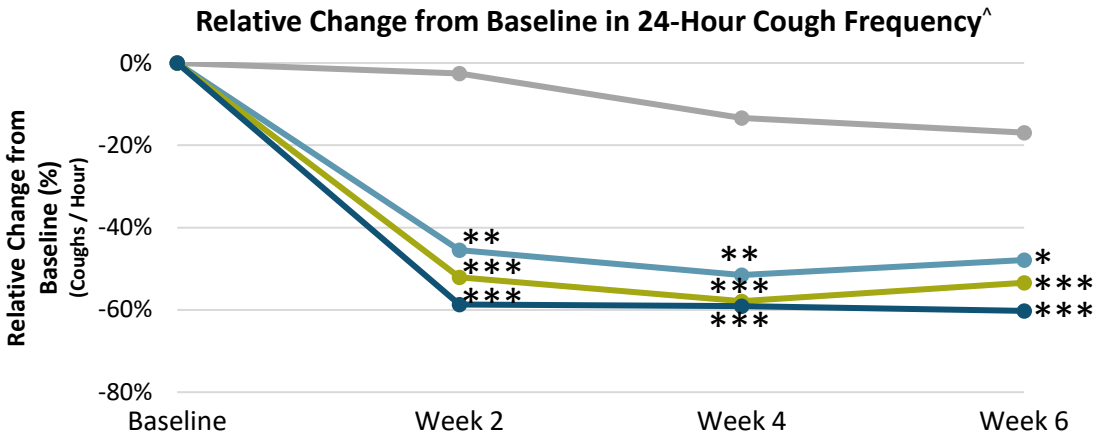
## Significant Reduction in Cough Frequency (Primary Endpoint)



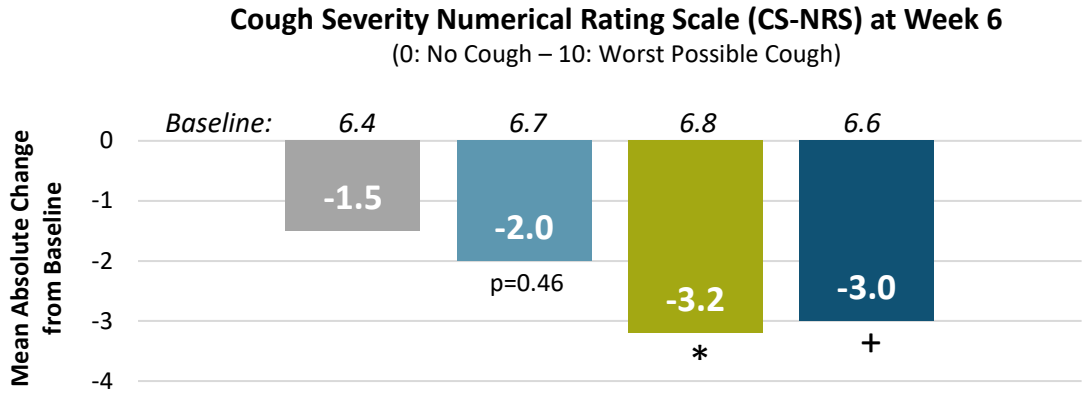

## Broad Coverage Clinically Meaningful Response




## Rapid and Persistent Cough Reduction




## Significant Reduction in Patient-Reported Outcomes with 54 mg BID




Placebo (N = 39) | 27 mg BID (N = 42) | 54 mg BID (N = 43) | 108 mg BID (N = 40)

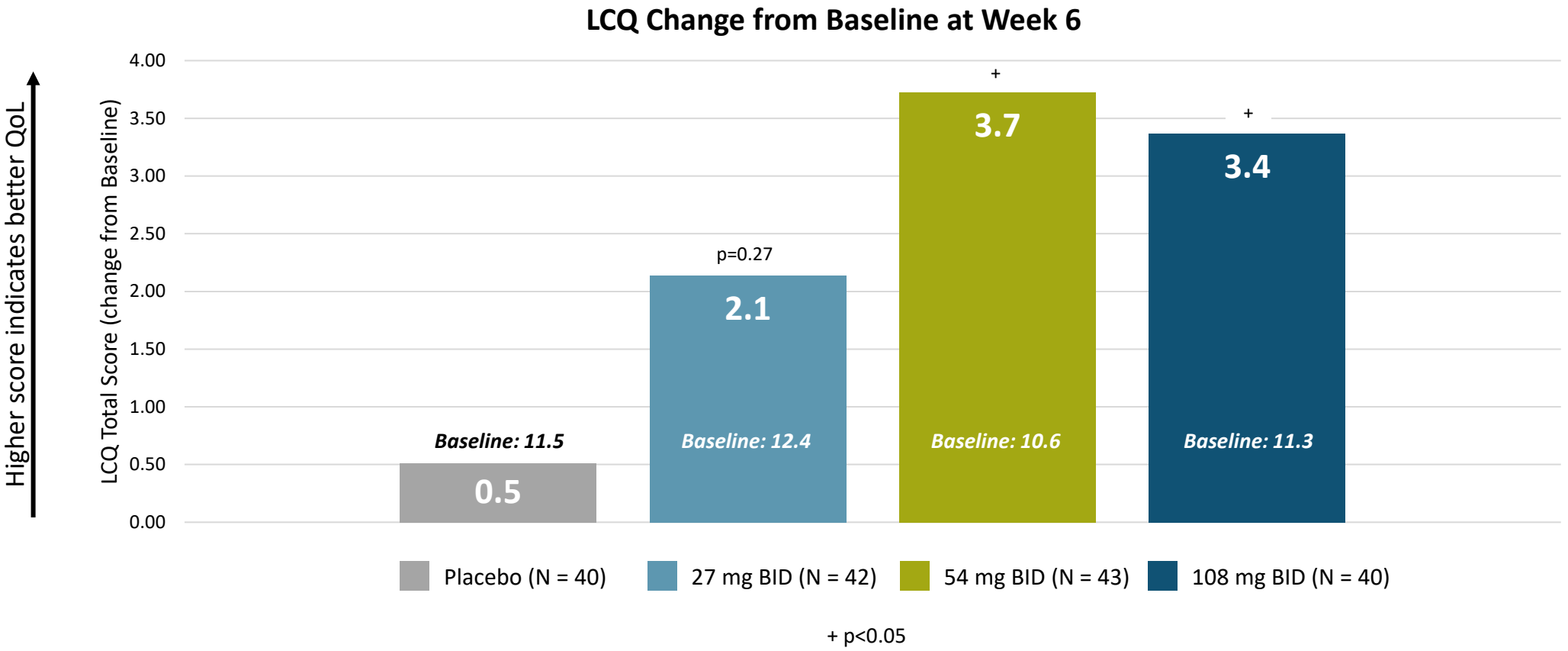
NAL ER / nalbuphine ER is an investigational therapy
mITT population, Primary efficacy analysis conducted on log-transformed cough frequency data, PBO = placebo
^One placebo patient with an extreme outlier value at Week 6 was excluded from the modified intent-to-treat (mITT) population. Inclusion of the patient in the placebo group would have resulted in an increased cough frequency from baseline in the placebo group and much greater placebo-adjusted differences.
Responder is defined as those subjects meeting the pre-specified thresholds of a 30%, 50%, or 75% reduction from Baseline
Molyneaux P et al. JAMA 2026 doi: 10.1001/jama.2025.26179

+ p<0.05 * p<0.01 ** p<0.001 *** p<0.0001

# Significant Improvement in Patient-Reported Cough-Related Quality of Life

## *Change from Baseline in LCQ Total Score (higher score indicates better QoL)*

*An improvement of 1.3 units is considered clinically important on a 21-point scale*




Raj AA et al. Handb Exp Pharmacol 2009 doi: 10.1007/978-3-540-79842-2_16

LCQ: Leichester Cough Questionnaire

NAL ER / nalbuphine ER is an investigational therapy

# Summary of Common (≥ 5%) TEAEs by Dose Received at Onset of AE

***TEAEs most frequently occurred during the titration period at 27 mg***

CORAL

*Denominator is total placebo events (placebo) or Total Active events (active doses)*

| Preferred Term | Placebo (m = 63) n (%) | 27 mg BID (m = 208) n (%) | 54 mg BID (m = 94) n (%) | 108 mg BID (m = 73) n (%) | Total Active (m = 375) n (%) |
|---|---|---|---|---|---|
| Nausea | 2 (3.2) | 39 (10.4) | 7 (1.9) | 6 (1.6) | 52 (13.9) |
| Vomiting | 0 (0) | 15 (4.0) | 12 (3.2) | 11 (2.9) | 38 (10.1) |
| Dizziness | 2 (3.2) | 18 (4.8) | 6 (1.6) | 13 (3.5) | 37 (9.9) |
| Constipation | 0 (0) | 13 (3.5) | 7 (1.9) | 10 (2.7) | 30 (8.0) |

*Post-hoc analysis to determine onset of adverse event by actual dose received*

- Discontinuations due to TEAEs were **similarly distributed across the placebo (5.0%) and active (5.6%)** dose groups
- Majority of TEAEs were mild (Grade 1) or moderate (Grade 2) and consistent with prior NAL ER studies and the class of drug
  - Nausea, vomiting, constipation, dizziness, headache, and dry mouth all either Grade 1 or Grade 2 TEAEs
  - One patient at the 108 mg BID dose group reported Grade 3 TEAEs of fatigue and somnolence
- SAEs occurred in patients at a higher rate in the placebo dose group (10%) than the active dose group (1.6%)

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NAL ER / nalbuphine ER is an investigational therapy
Safety population
Number of events; one patient may have multiple treatment emergent adverse events
m: number of events
Table does not include TEAEs that occurred pre- or post-treatment

# IPF-Related Chronic Cough: OCEAN Phase 3 Program Trial Framework

OCEAN

| | *Screening Period* | Titration Period | Fixed-Dose Period | Safety Follow-Up Period |
|---|---|---|---|---|
| **OCEAN-1** | | **Weeks 1 - 2** | **Weeks 3 – 54**<br>24wk Primary Endpoint (PE) | **3 Weeks** |
| 2:1 Randomization | n = 204 | NAL ER 27 mg<br>QD → BID | NAL ER 54 mg BID | *No Treatment* |
| | n = 102 | Placebo<br>QD → BID | Placebo BID | |
| **OCEAN-2** | | **Weeks 1 - 2** | **Weeks 3 – 14**<br>12wk PE | **3 Weeks** |
| 2:1 Randomization | n = 134 | NAL ER 27 mg<br>QD → BID | NAL ER 54 mg BID | *No Treatment* |
| | n = 67 | Placebo<br>QD → BID | Placebo BID | |

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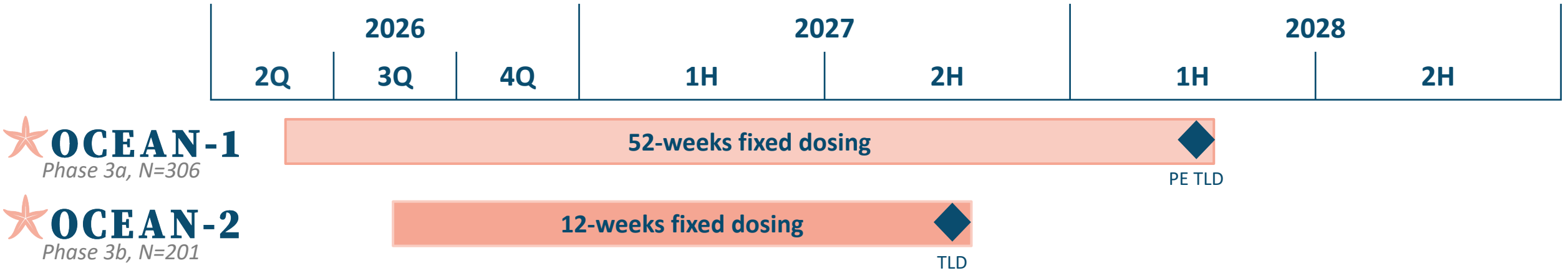
# IPF-Related Chronic Cough: OCEAN Phase 3 Clinical Program Overview




### Multinational Trial

**OCEAN-1:** ~80-90 sites in US, Canada, Spain, Poland, & UK

- ~60-70% of subjects enrolled to be US-based

**OCEAN-2:** ~70-80 sites in US, Canada, & UK

### Primary Efficacy Endpoint

**Relative change from Baseline in objective 24-hour cough frequency for NAL ER compared with placebo**

- **OCEAN-1:** at 24 weeks of fixed dosing
- **OCEAN-2:** at 12 weeks of fixed dosing

*As measured by the VitaloJAK® Cough Monitor*

### OCEAN-1 Key Secondary Endpoints

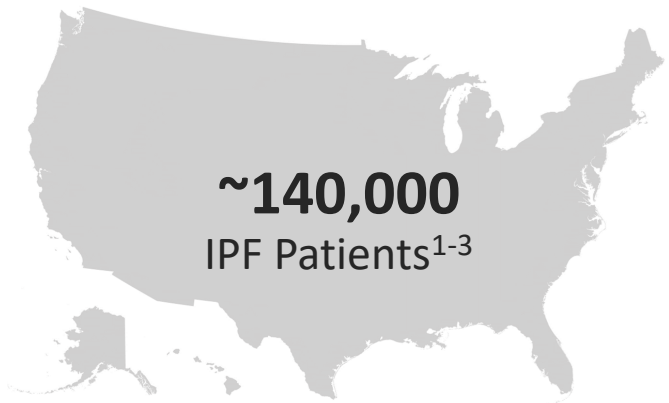
- Δ from Baseline in the CS-NRS* at Week 26
- Δ from Baseline in 24-hour objective cough frequency at Week 6
- Proportion achieving ≥50% reduction from Baseline in 24-hour objective cough frequency at Week 26
- Δ from Baseline in the E:RS-IPF Cough domain at Week 26
- Proportion of participants achieving a ≥3-point improvement from Baseline in CS-NRS at Week 26
- Δ from Baseline in the E:RS-IPF Breathlessness domain at Week 26

CS-NRS: Cough Severity Numerical Rating Scale, E-RS:IPF: Evaluating Respiratory Symptoms: Idiopathic Pulmonary Fibrosis, PE: Primary Endpoint, TLD: Topline Data

**will be first key secondary in OCEAN-2*

# Leading with IPF Specialty Indication with a High Unmet Need and Favorable Commercial Dynamics

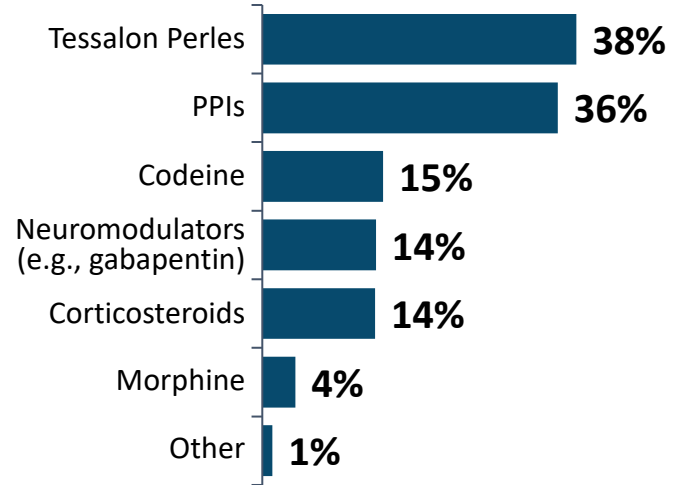
## US IPF Opportunity Today




**+7-10%** YoY IPF category growth[1-3]

**60-70%** Avg. % of patients with uncontrolled chronic cough

## IPF Cough Treatment Paradigm[4]

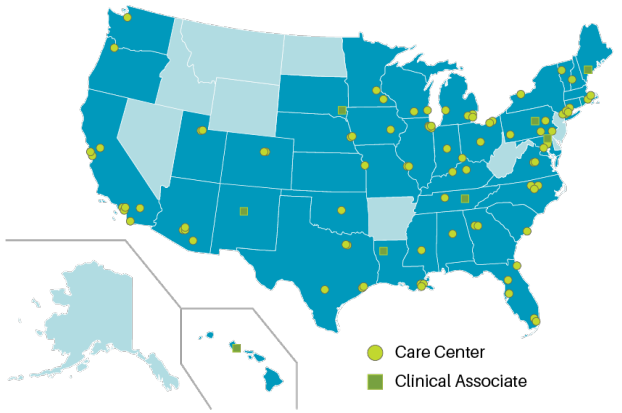



**No FDA-approved therapies for IPF patients with chronic cough**

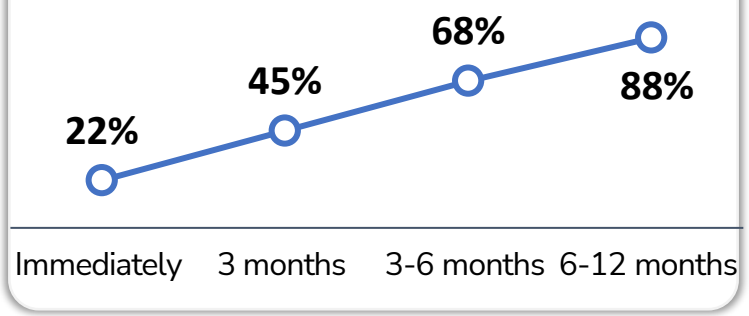
**Antifibrotics have failed to show a benefit on cough reduction[5,6]**

## Expected Commercial Model

**90+ ILD Care Centers in the US Covered by 50-75 Reps**




### Rapid Potential Prescribing Uptake[8]

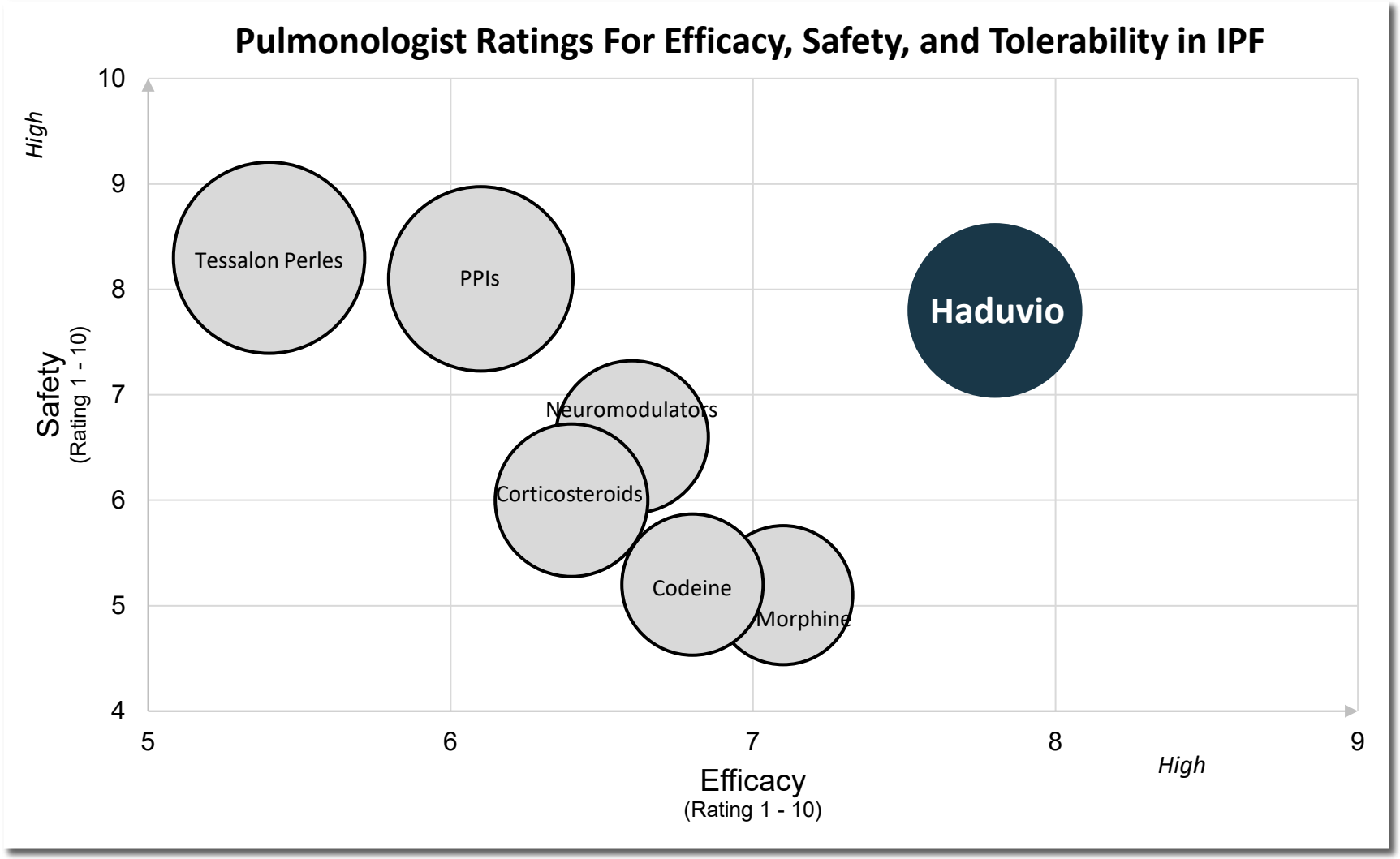



YoY: Year-on-year, PPI: proton-pump inhibitors

[1]Raghu G et al. ERJ 2016 doi: 10.1183/13993003.01653-2015 [2]Raghu G et al. Lancet Respir Med 2014 doi: 10.1016/S2213-2600(14)70101-8 [3]U.S. Census NC-EST2023-AGESEX-RES [4]Indegene Market Research US 2022 n=45
[5]vanManen MJG et al. ERJ 2017 doi: 10.1183/13993003.01157-2017 [6]vanManen M ERJ 2016 doi: 10.1183/13993003.congress-2016.PA785 [7]Pulmonary Fibrosis Foundation, accessed June 1, 2025 [8]LCP US Pulmonologist Market Research 2025 n=90

Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

# Pulmonologists Perceive Haduvio Having Greater Efficacy with Comparable Safety and Tolerability



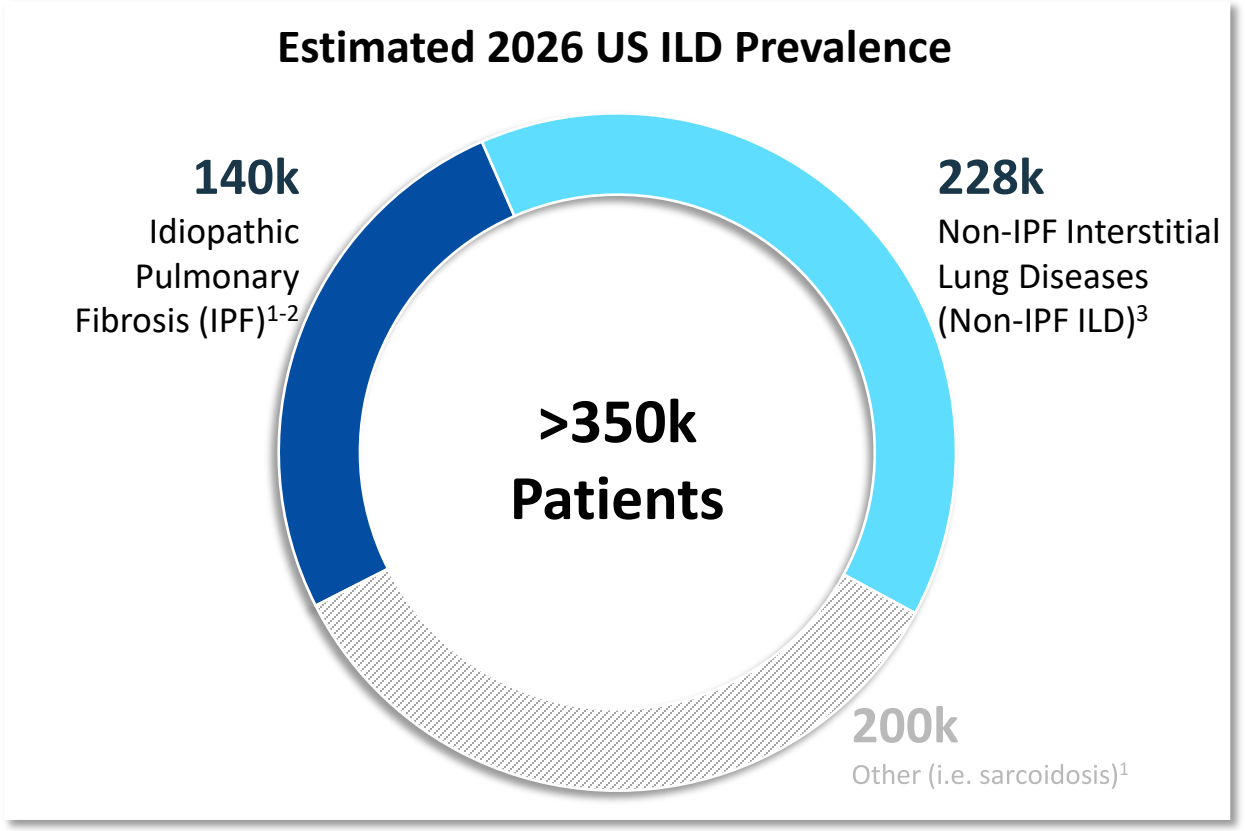

*"This drug should become a **standard treatment option for cough in IPF** because there is a significant unmet need. **Current antifibrotic therapies do not effectively address cough.** Therefore, if an IPF patient has cough despite being on antifibrotics, this new drug should appear early in treatment algorithms or guidelines, essentially as a first-line option for managing cough"*

**- IPF Specialist, CT**

LCP US Pulmonologist Market Research, 2025 n=90; assessments based on target product profile from Ph2b CORAL data
Size of bubble indicates tolerability rating 1 - 10
Responses weighted by number of IPF patients, similar trends with raw scores and unweighted averages
Abbreviations: PPI's, Proton Pump Inhibitors
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

# Non-IPF ILD-Related Chronic Cough Represents a Large, Untreated, and Underserved Population

***Expansion Into Non-IPF ILD More Than Doubles the Addressable Patient Population***




ILDs encompass over 200 indications with common fibrosis

## Patients with Non-IPF ILD-related chronic cough are similar to patients with IPF-related chronic cough[4,5]

- Underlying lung fibrosis
- 50-60% have uncontrolled chronic cough
- No approved therapies for chronic cough
- High negative impact on QoL

## Next Steps

- Plan to initiate an adaptive Phase 2/3 clinical trial in 2H 2026, subject to FDA discussion and review of the protocol

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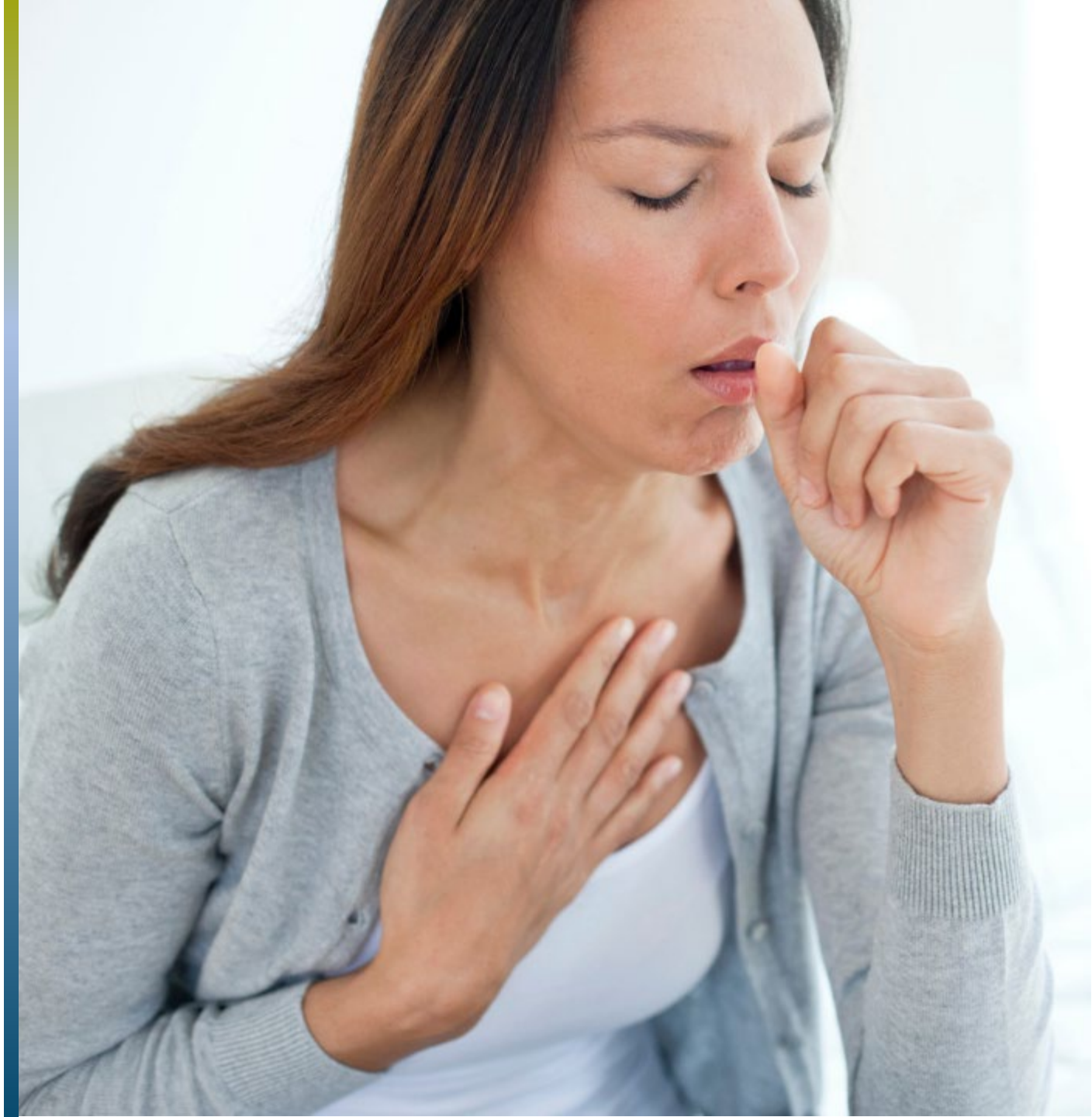
[1]Raghu G et al. Lancet Respir Med 2014 doi: 10.1016/S2213-2600(14)70101-8 [2]Raghu G et al. Lancet Respir Med 2016 doi: 10.1016/S2213-2600(16)30222-3 [3]Trevi Internal Analysis [4]Based on Pulmonologists who managed Non-IPF ILD patients with chronic cough in the last 12 months, June 2022 (N=30) [5]Kolb M et al. Respir Res 2019 doi: 10.1186/s12931-019-1022-1
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

# Refractory Chronic Cough (RCC)



# Refractory Chronic Cough Carries a High Burden of Disease and Impact on Patients' Lives

No FDA-approved therapies

61% have anxiety and/or depression

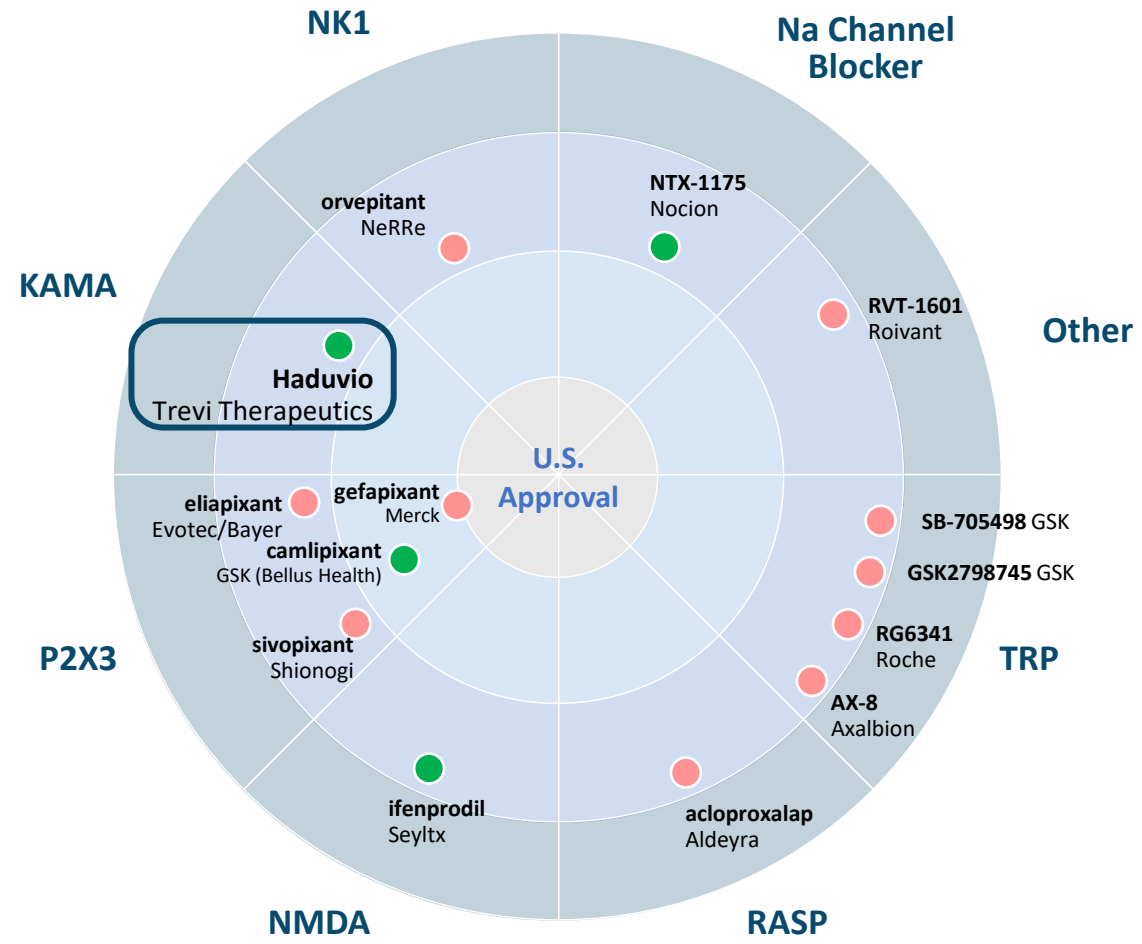
34% reduction in work activities
30% reduction in non-work activities

Impaired physical and psychological health

~2 in 3 women with chronic cough experience cough-induced urinary incontinence

Sources: Hull JH et al., ERJ Open Res 2021, Dicpinigaitis PV et al., Lancet Respir Med 2024, Smith JA et al, Respir Res 2024 doi.org/10.1186/s12931-024-02881-4, Puente-Maestu L et al, ERJ Open Res 2023 doi.org/10.1183/23120541.00425-2023, Gibson P et al, Chest 2016 doi:10.1378/chest.15-1496, Brister D et al. Lung 2024 DOI: 10.1007/s00408-024-00714-1
Modified from Figure 3 in Key A.L., et al Cough 2010 doi: 10.1186/1745-9974-6-4 used under CC BY 2.0.
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

# Haduvio's Central and Peripheral Mechanism Has Best-in-Class Potential in RCC



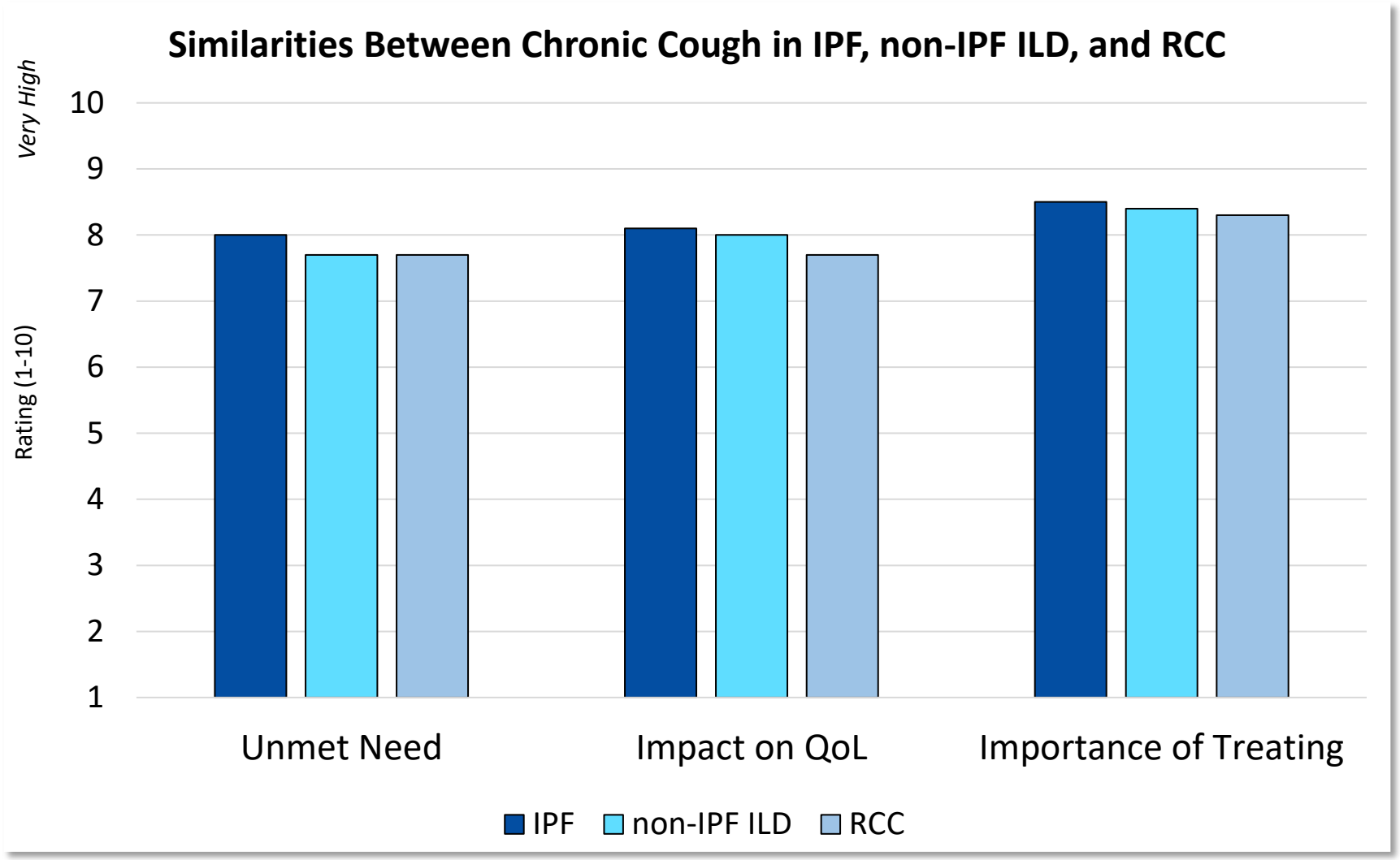

## Haduvio has an opportunity to be second-to-market in a category with a high unmet need where many mechanisms have failed

- Differentiated central and peripheral mechanism
- Achieved a deep, broad, and rapid effect in clinical trials to date
- Statistically significant across a wide range of baseline cough counts
- Reduction in objective cough counts supported by patient-reported outcomes observed in clinical trials

Sources: Haduvio, Trevi Therapeutics: Trevi Therapeutics Press Release March 10, 2025, Orvepitant, NeRRe: NeRRe Therapeutics Press Release July 7, 2021, NTX-1175, Nocion: Nocion Therapeutics Press Release November 18, 2024, RVT-1601, Roivant Sciences: doi: 10.1016/S2213-2600(17)30310-7, RG6341, Roche: Roche YTD September 2024 Sales Presentation, AX-8, Axalbion: Axalbion ACC Presentation 2025, Acloproxalap, Aldeyra: Aldeyra Press Release January 4, 2024, Ifenprodil, Seyltx: Seyltx Press Release July 16, 2024, Sivopixant, Shionogi: doi: 10.1007/s00408-022-00592-5, Camlipixant, GSK: GSK Annual Report 2024, Gefapixant, Merck: Merck Press Release December 20, 2023, Eliapixant, Evotec/Bayer: Bayer Press Release February 4, 2022

Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

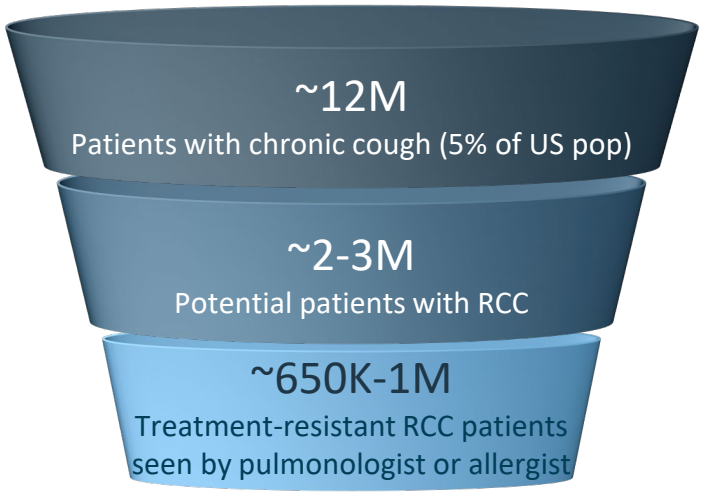
# Physicians Recognize the High Unmet Need, QoL, and Importance of Treating in Refractory Chronic Cough




Indegene Market Research 2022 (n=45)

# Specialty-Focused Commercial Model Efficiently Targets Treatment-Resistant RCC Patients

## US RCC Opportunity

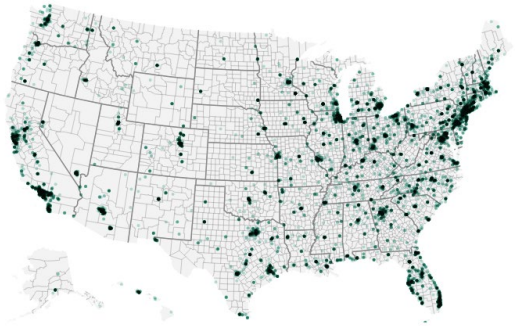



**Focus on treatment failures:**

- **Highest unmet need**
- **Maintain specialty pricing across IPF, non-IPF ILD, and RCC**

## RCC Commercial Model

**Plan to target pulmonologists and allergists would provide significant overlap with ILD centers**



**~1/3 RCC patients see a pulmonologist or allergist**

**Efficient proposed sales model with IPF/non-IPF ILD**

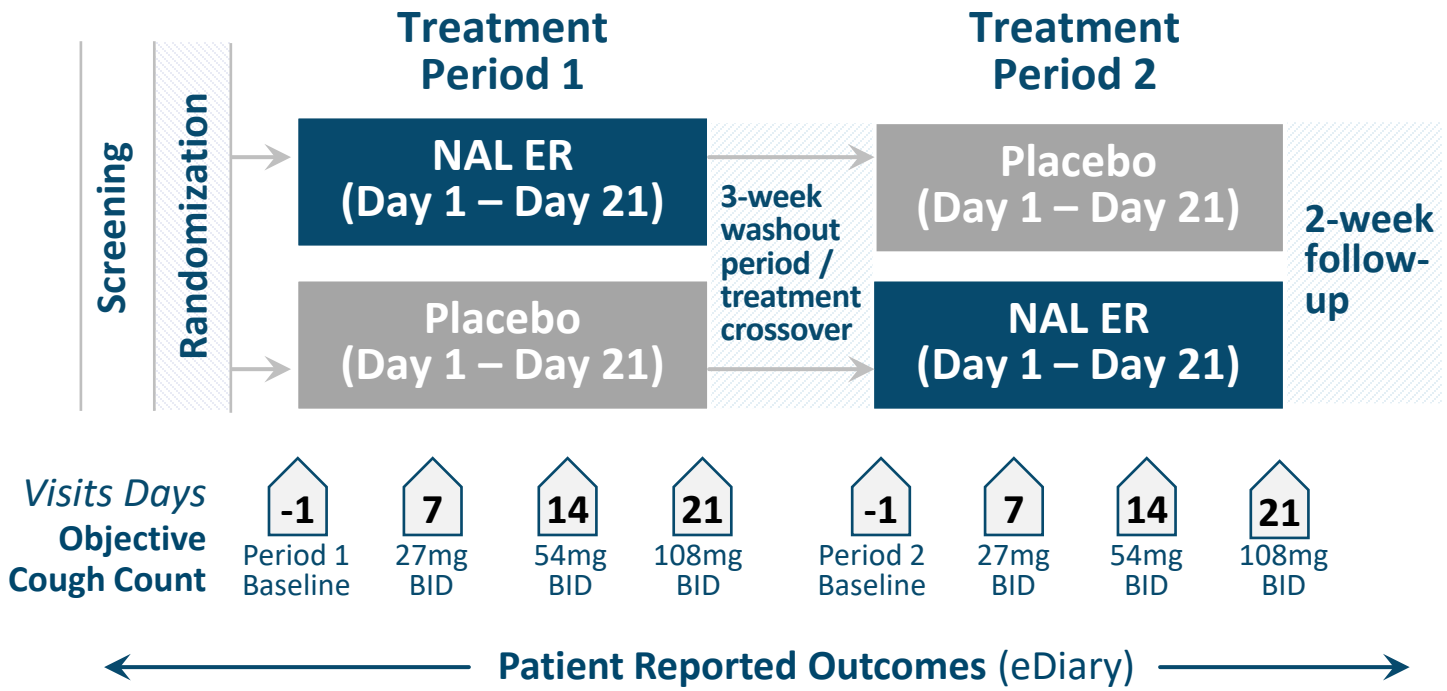
## RCC Prescribing Drivers

1. Efficacy
2. Speed of Effect
3. Safety

**Efficacy and Safety expected to drive physician prescribing in RCC, similar to other indications**

RCC Opportunity: DOI: 10.1016/j.jaip.2021.07.022, DOI: 10.1177/00368504241238080, LifeSci Patient Survey 2022 (N=1,000)
Pulmonologist map: HealthLink Dimensions data
RCC Prescribing Drivers: Indegene US Market Research 2024 (n = 152), Prescribing trends are similar across specialty
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

# RIVER Phase 2a Clinical Trial in RCC (N=66)




**Subgroups** (24-hour cough frequency):
≥20 coughs/hour
10–19 coughs/hour

## Primary Efficacy Endpoint

- 24-hour cough frequency using objective cough monitor

VitaloJAK® Cough Monitor

## Secondary Endpoints

- Patient-Reported Cough Frequency (PR-CF)*
- CS-VAS*
- LCQ
- PGI-S, PGI-C Cough
- CGI-S, CGI-C Cough

*Selected data included in topline results
BID: twice daily, CS-VAS: cough severity visual analog scale, LCQ: Leicester cough questionnaire, PGI-S: patient global impression of cough severity, PGI-C: patient global impression of change in cough, CGI-S: clinician global impression of cough severity, CGI-C: clinician global impression of change of cough
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy
Clinicaltrials.gov ID: NCT05962151

# Baseline Characteristics of 66 Randomized Patients

## **Cough Severity** (VAS, mm)

**Mean (SD): 72.2 (13.3)**

## Cough Frequency

**Mean (SD): 34.7 (29.2)**
(coughs/hour)

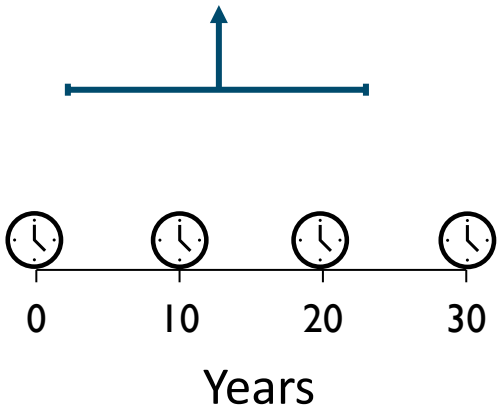
**>800 coughs/day**

## **Body mass index** ($kg/m^2$)

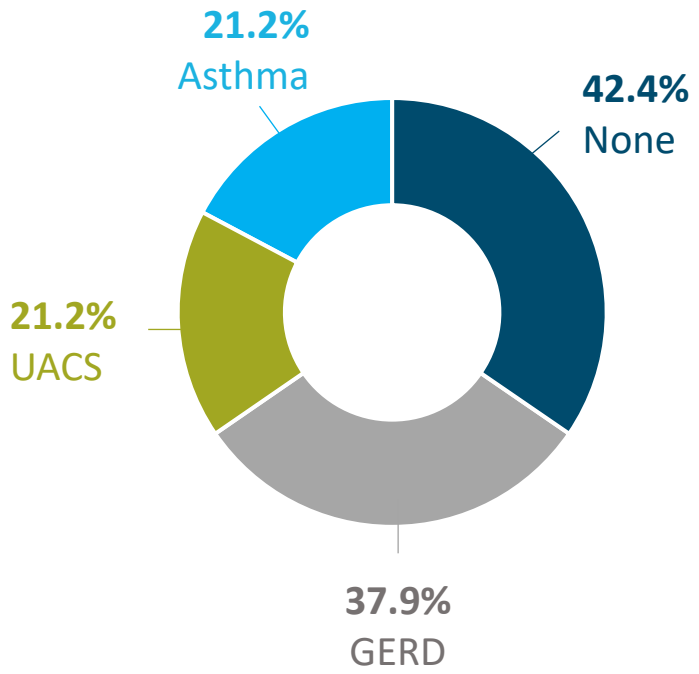
**Mean (SD): 29.0 (5.4)**

## Duration of Cough

**Mean (SD):**
**12.6 (10.4) years**



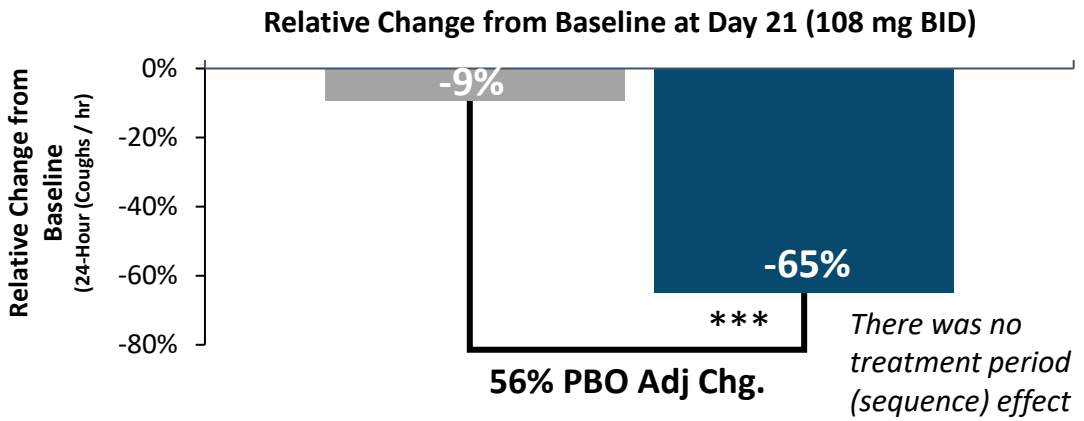

## Cough-associated Medical Conditions



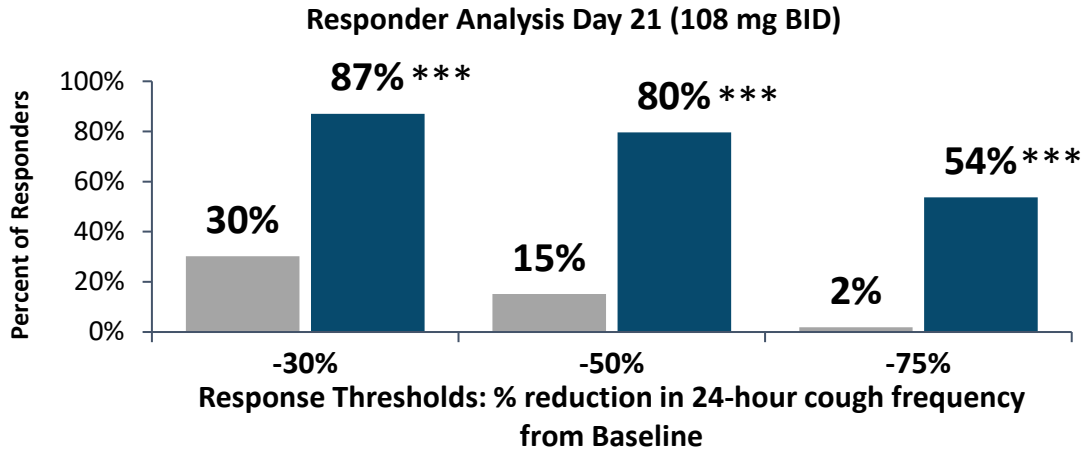

For duration of cough, the total number of years is determined by dividing the total number of days by 365.25. Missing date part values were imputed as follows. When day is missing, the last day of the month is assumed. When day and month are missing, December 31st is assumed. UACS history is taken from the Medical History CRF page and coded using MedDRA version 27.0. For each specific cough-associated medical condition, patients are included only once, even if they have a history of multiple events in that specific medical condition
GERD, gastroesophageal reflux disease; h, hour; SD, standard deviation; UACS, upper airway cough syndrome; VAS, visual analog score.

# Large, Broad, and Rapid Effect Observed in RIVER Phase 2a Trial in RCC

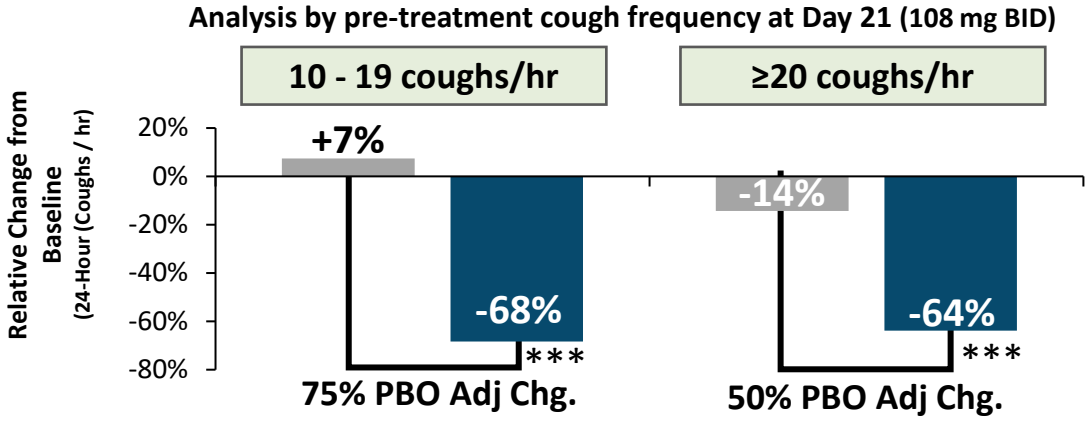
## Significant Reduction in Cough Frequency (Primary Endpoint)



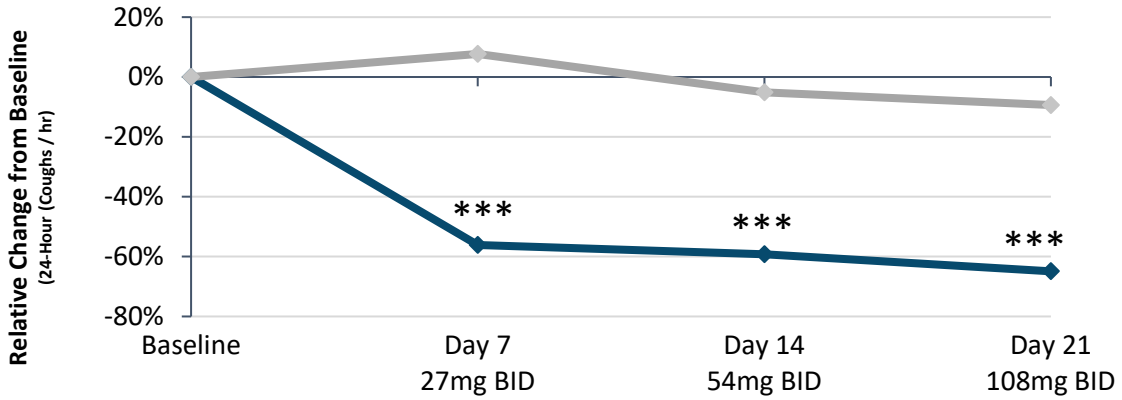

## Broad Coverage Clinically Meaningful Response




## Consistent Effect Across a Broad Range of Baseline Cough Counts




## Rapid Onset - As Early as Day 7, Lowest Dose




NAL ER  Placebo  ***p<0.0001

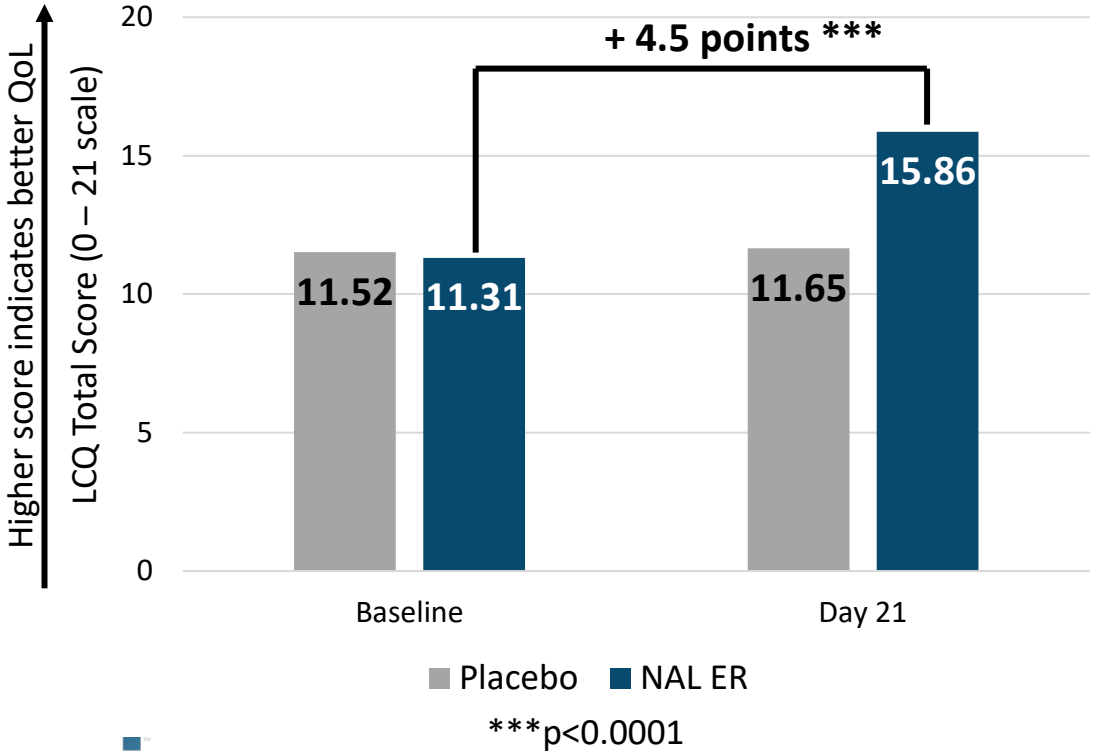
Primary efficacy analysis conducted on log-transformed cough frequency data
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy
All graphs: Change from Baseline, Responder Analysis and Rapid Onset all conducted on the FAS population.

# Patient-Reported Cough-Related Quality of Life

## *Change from Baseline in LCQ Total Score (higher score indicates better QoL)*

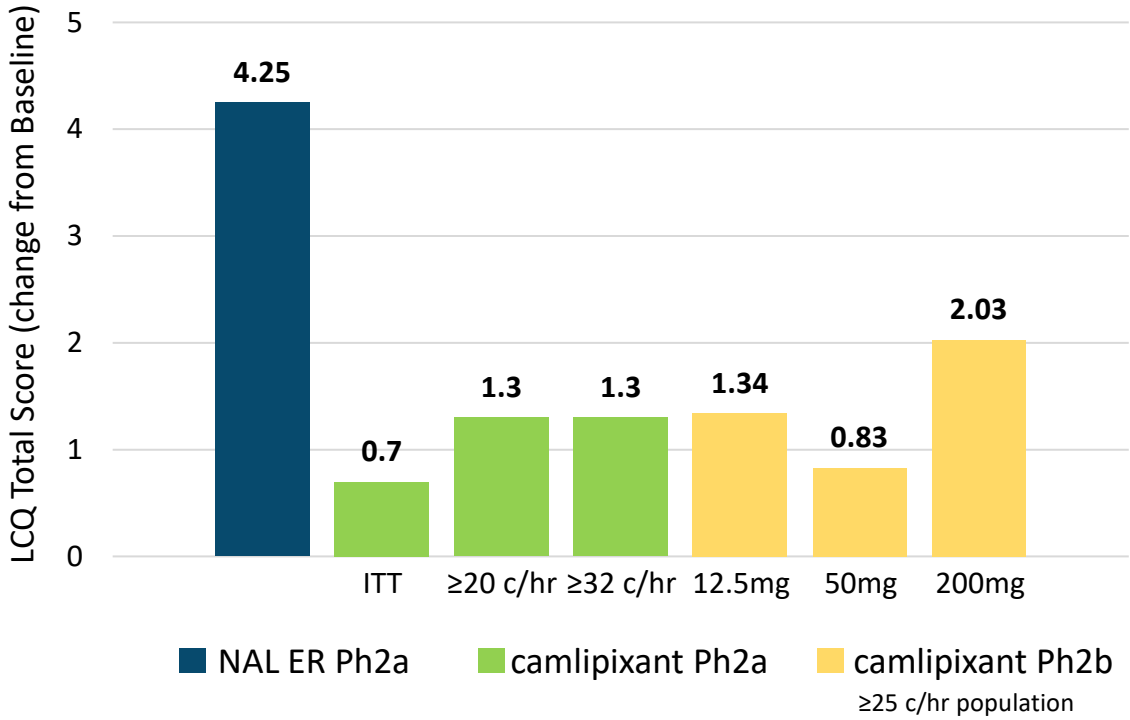
*An improvement of 1.3 units is considered clinically important on a 21-point scale*

### RIVER NAL ER LCQ Total Score




### LCQ Total Score Placebo Adjusted Change

NAL ER comparison to camlipixant




Note: This is a cross-trial comparison rather than a head-to-head clinical trial, and the data may not be directly comparable due to differences in trial designs and methodologies. ITT: intention-to-treat

Raj AA et al. Handb Exp Pharmacol 2009 doi: 10.1007/978-3-540-79842-2_16, Smith JA et al. AJRCCM 2025 doi: 10.1164/rccm.202501-0093RL, Smith JA et al. AJRCCM 2025 doi: 10.1164/rccm.202409-1752OC

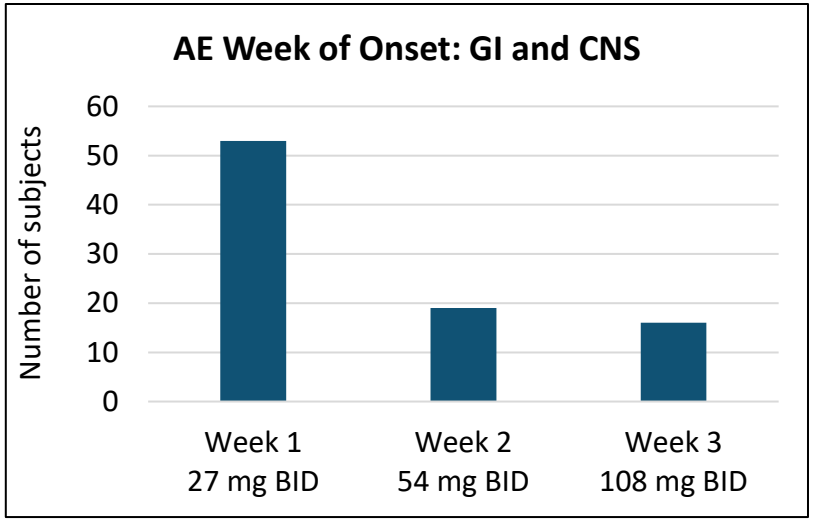
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

# Summary of Treatment-Emergent Adverse Events by Preferred Term

| Treatment-Emergent Adverse Events at ≥10% Frequency | Placebo N=59 n (%) | NAL ER N=63 n (%) |
|---|---|---|
| Constipation | 4 (6.8) | 18 (28.6) |
| Somnolence | 0 (0) | 16 (25.4) |
| Nausea | 2 (3.4) | 14 (22.2) |
| Dizziness | 2 (3.4) | 12 (19.0) |
| Headache | 7 (11.9) | 10 (15.9) |
| Fatigue | 3 (5.1) | 9 (14.3) |

There were no treatment emergent serious adverse events
Six patients experienced treatment-emergent AEs that were CTCAE Grade 3:
Haduvio (4 patients): Somnolence, dizziness, headache, hypoaesthesia, lethargy, nephrolithiasis
Placebo (2 patients): Headache and blepharitis
*There were no CTCAE treatment-emergent AEs above Grade 3*

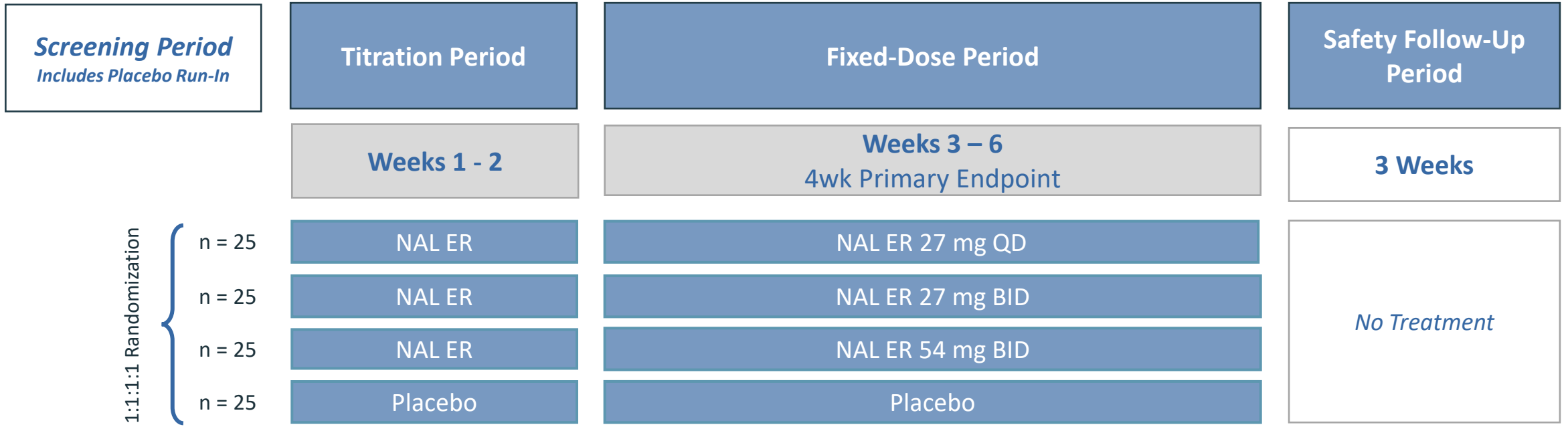
| | Total (N = 66) |
|---|---|
| Discontinued Treatment, n (%) | 15 (22.7%) |
| Adverse Event | 10 (15.2%) |
| Withdrawal by Subject | 4 (6.1%) |
| Other | 1 (1.5%) |



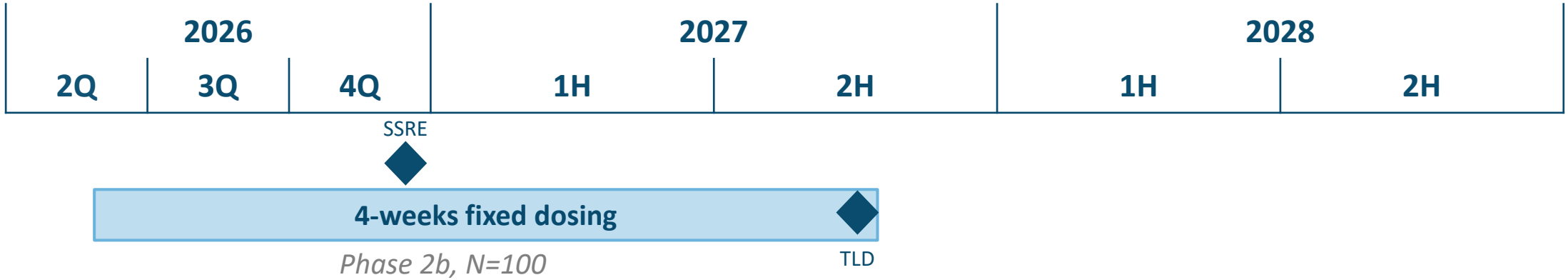

Safety Population
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy
Subject is included only once, even if they experienced multiple events in that preferred term

# Refractory Chronic Cough: Phase 2b Trial Framework

***A Randomized, Double-Blind, Placebo-Controlled Dose-Ranging Study to Evaluate the Efficacy and Safety of Nalbuphine Extended-Release Tablets for the Treatment of Patients with Refractory Chronic Cough***



# Refractory Chronic Cough: LAKE Phase 2b Trial Overview




**Assumptions:**

- 27 mg QD, 27 mg BID, 54 mg BID, PBO
  - 1:1:1:1 randomization
- ~40 sites in UK, Canada, & Poland

**Primary Endpoint**

**Relative change from Baseline in objective 24-hour cough frequency for NAL ER compared with placebo at Week 6**

*As measured by the VitaloJAK® Cough Monitor*

**PRO Secondary Endpoints**

***Assessed changes from Baseline, measured at week 6 and other prespecified timepoints***

- Patient-Reported Cough Frequency
- Cough Severity Visual Analog Scale
- McMaster Cough Severity Questionnaire
- Leicester Cough Questionnaire©
- Patient Global Impression of Severity
- Patient Global Impression of Change
- Incontinence Questionnaire – Urinary Incontinence Short Form

PRO: Patient-Reported Outcome, SSRE: Sample Size Re-Estimation, TLD: Topline Data

# Haduvio Represents a Potential $6B+ Peak Sales Opportunity Across Chronic Cough Indications

| | IPF | Non-IPF ILD | Treatment Resistant RCC (TR-RCC) | Total |
|---|---|---|---|---|
| Est. U.S. 2026 Patients | 140K | 228K | 650K – 1M | |
| Eligible Patients | 80 – 105K | 115 – 135K | 650K – 1M | 850K – 1.2M |
| Share Assumptions | 25 – 35% | 20 – 30% | 3 – 5% | |

Key Factors in Determining Total Addressable Markets

**Addressable Patients**
Uncontrolled Chronic Cough Patients

**WAC Price**
Specialty Pricing

**Gross-To-Net**
Minimal to No Contracting
25-30% GTN

| | IPF | Non-IPF ILD | TR-RCC | Total |
|---|---|---|---|---|
| **Haduvio U.S. Peak Sales Est.** Based on Net Sales | **$2B – $4B** | **$2B – $4B** | **$2B – $5B** | **$6B+** |

IPF: [1]Raghu G et al. Lancet Respir Med 2014 doi: 10.1016/S2213-2600(14)70101-8 [2]Raghu G et al. Lancet Respir Med 2016 doi: 10.1016/S2213-2600(16)30222-3 [3]Trushenko NV et al. Diagnostics 2025 doi: 10.3390/diagnostics15091139 [4]Based on Pulmonologists who managed Non-IPF PF-ILD patients with chronic cough in the last 12 months, June 2022 (N=30) [5]LCP US Pulmonologist Market Research 2025 n=90 [6]LCP US Payer Market Research 2025 n=15
Non-IPF ILD: [7]Trevi Internal Analysis [7]Based on Pulmonologists who managed Non-IPF ILD patients with chronic cough in the last 12 months, June 2022 (N=30) [8]LCP US Payer Market Research 2025 n=15
RCC: [9]Meltzer EO et al. JACI Pract 2021 doi: 10.1016/j.jaip.2021.07.022. [10]van Boemmel-Gemann S et al. Sage J 2024 doi: 10.1177/00368504241238080 [11]LifeSci Patient Survey 2022 (N=1,000) [12]Indegene US Market Research 2024 (n = 152) [13]Primal Access Feb 2025 (N=5)
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

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# Robust IP Portfolio Potentially Extends Protection Into 2040s
# Worldwide IP Filed

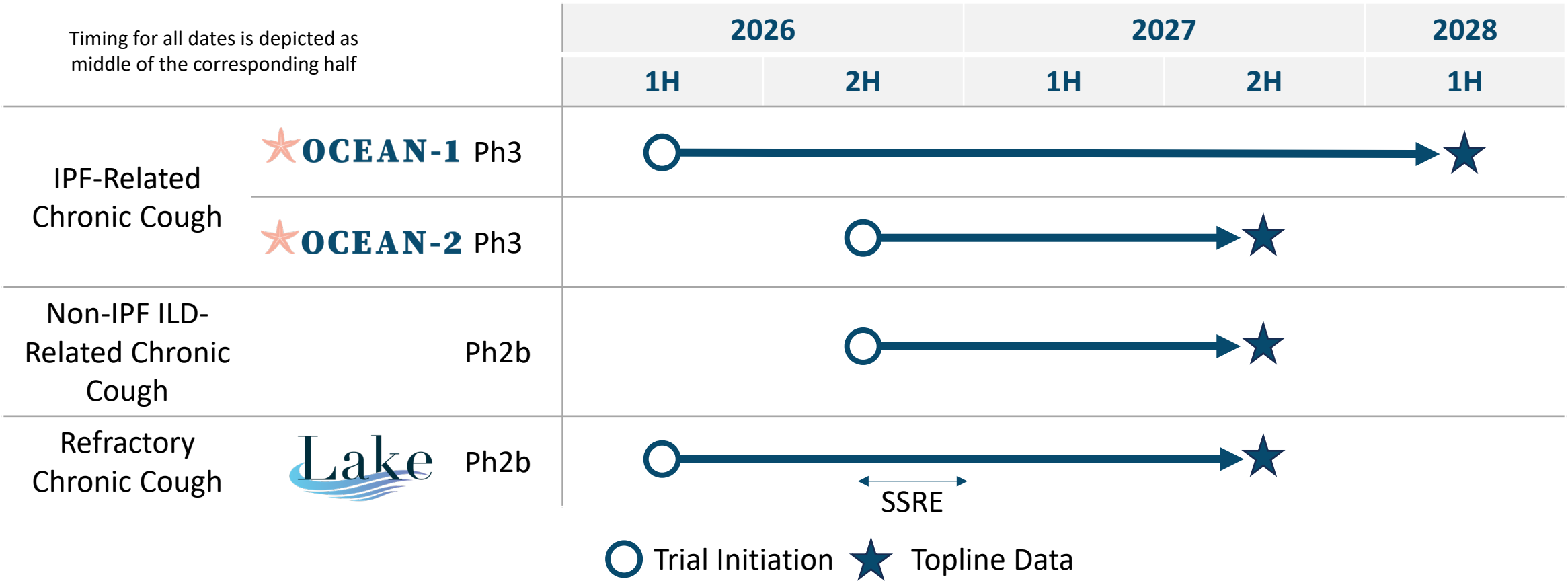
- Foundational Method of Use Protection
  - Broad claims defend against ANDA and 505(b)(2) competition
  - Chronic Cough in IPF
    - Issued U.S. patent (expires 2039)
    - Granted European patent (expires 2039)
  - Pipeline Indications (In prosecution)
    - Chronic cough in non-IPF ILD
    - Refractory chronic cough

    Expected protection to 2039 (if issued)

- Label-Driven IP Strategy
  - Special Populations
    - Hepatically impaired dosing: Issued U.S. patent (expires 2041)
    - Possible new IP based on Phase 1 studies
  - Additional label-driven applications filed or being developed that, if issued, will extend IP to 2047

## Additional IP Based on CMC and Clinical Development

# Expected Key Clinical Milestones and Data Readouts




**Cash, Cash Equivalents and Marketable Securities:**

$172M in cash, cash equivalents and marketable securities as of 3/31/26 together with the $162M of net proceeds from a follow-on underwritten common stock offering in April 2026 extends estimated cash runway into 2030[1].

Development plans and estimated dates are subject to discussions with regulatory authorities
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy
[1]The Company expects its current cash, cash equivalents and marketable securities to fund the development of Haduvio for the treatment of patients with IPF-related chronic cough, potentially through FDA approval. The Company also expects these cash resources will enable the Company to fund and report topline data from the planned Phase 2b clinical trial and potentially a subsequent Phase 3 trial for the treatment of patients with non-IPF ILD-related chronic cough, and the planned Phase 2b trial for the treatment of patients with RCC. The planned spending of these resources does not include any commercial expenses related to the commercial launch of Haduvio or any other clinical trials.