trevi® THERAPEUTICS

Controlling cough where it counts™

Corporate Presentation

March 2026

Nasdaq: TRVI

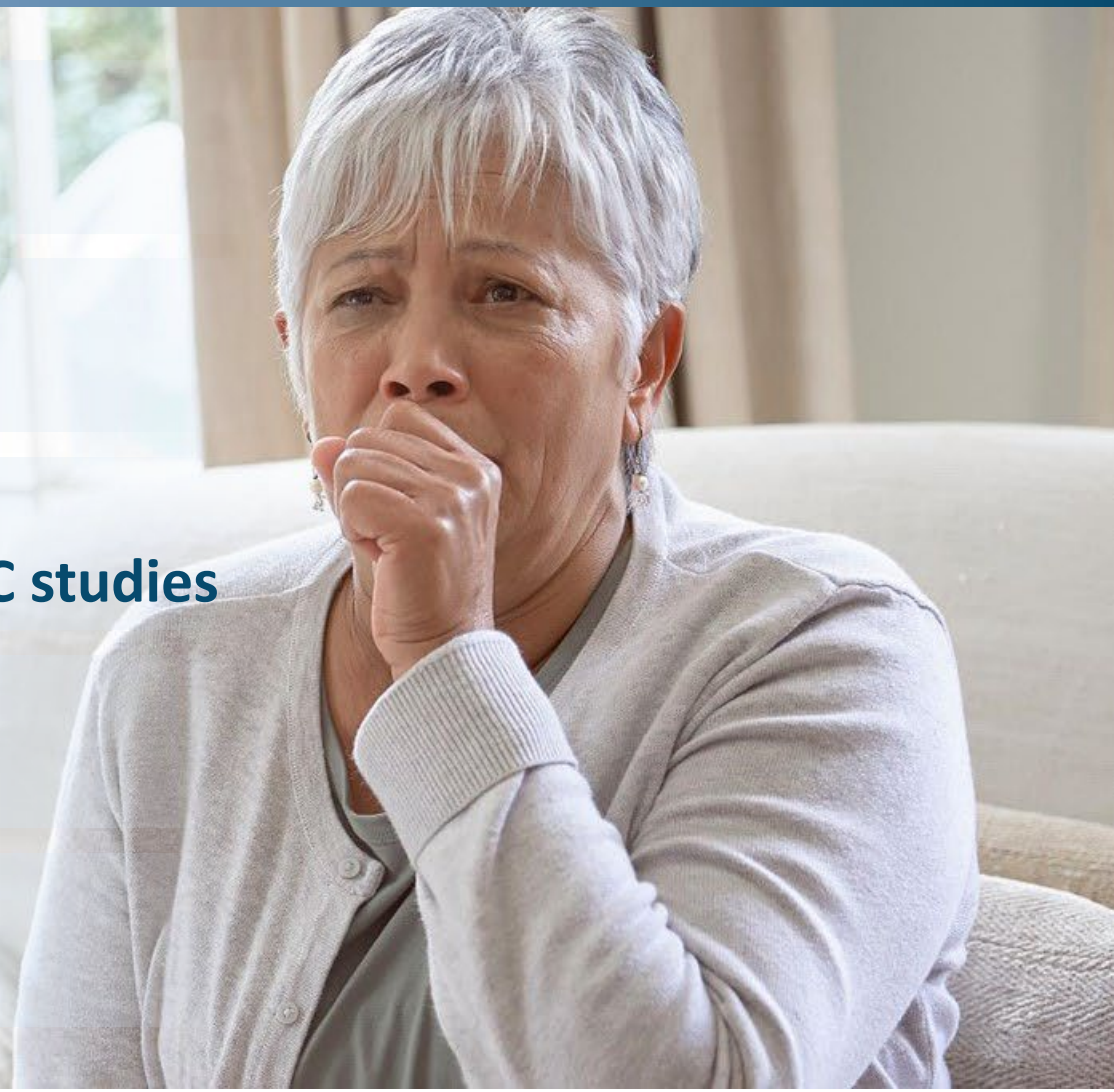
Forward Looking Statement Disclaimer

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 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 annual report on Form 10-K for the year ended December 31, 2025 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.

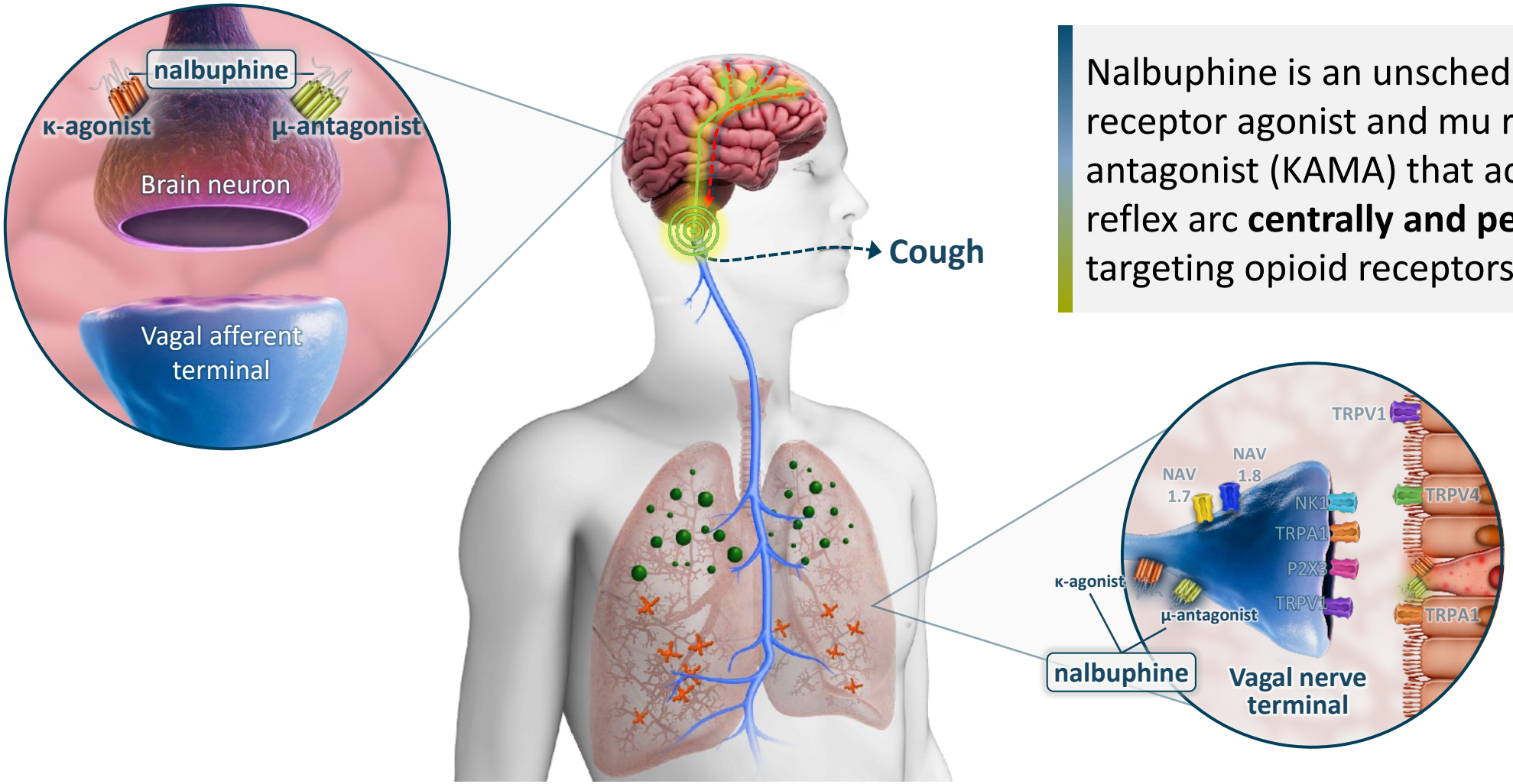
Best-in-Class Potential for Haduvio (nalbuphine ER) Across Difficult to Treat Chronic Cough Conditions

- Significant unmet need*
- Differentiated central and peripheral MOA
- Only investigational therapy with positive results in IPF-related chronic cough and RCC studies
- Specialty pricing and sales model
- $5B+ 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



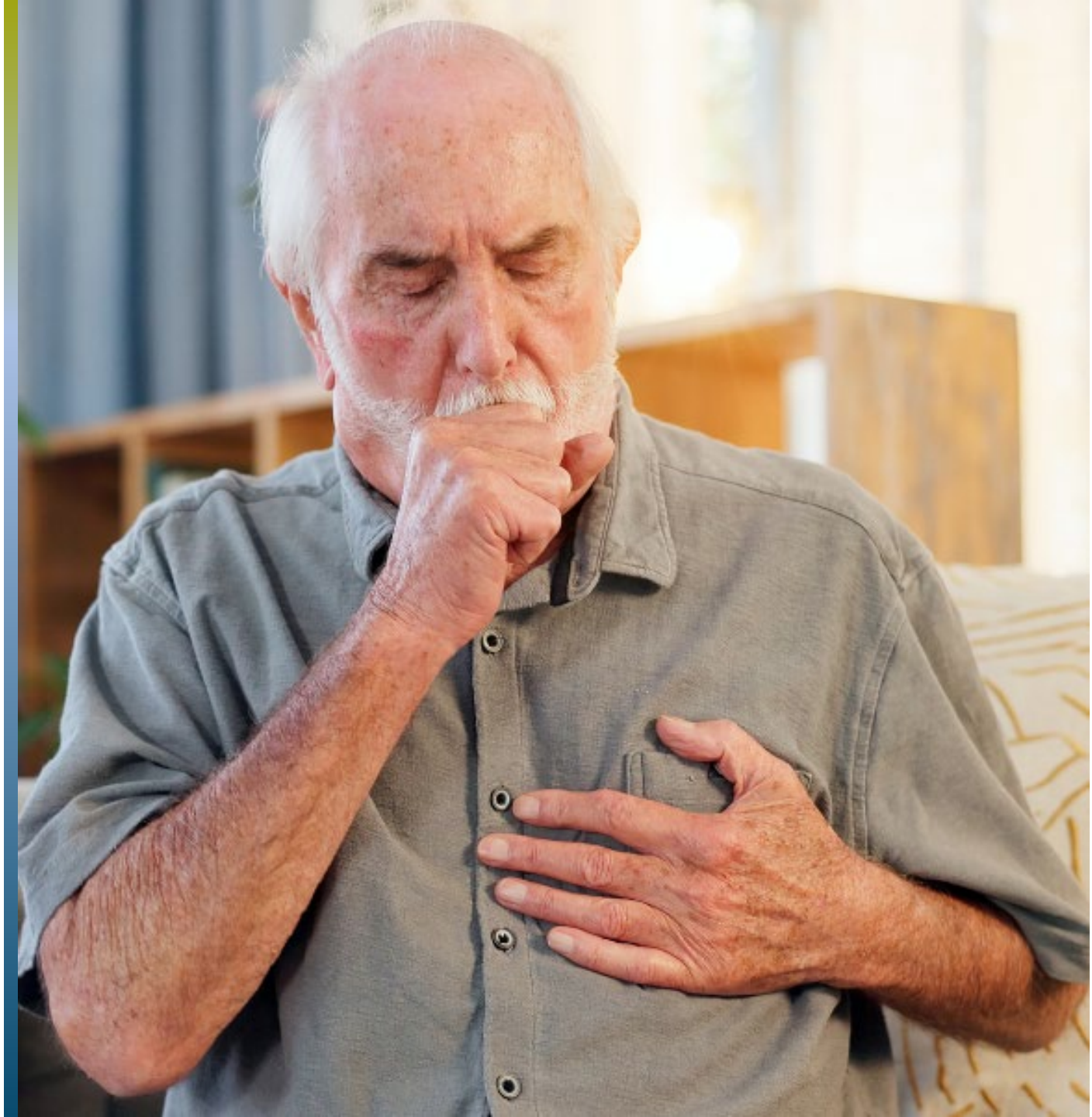
Nalbuphine is an unscheduled kappa receptor agonist and mu receptor antagonist (KAMA) that acts on the cough reflex arc **centrally and peripherally** by targeting opioid receptors involved in cough

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

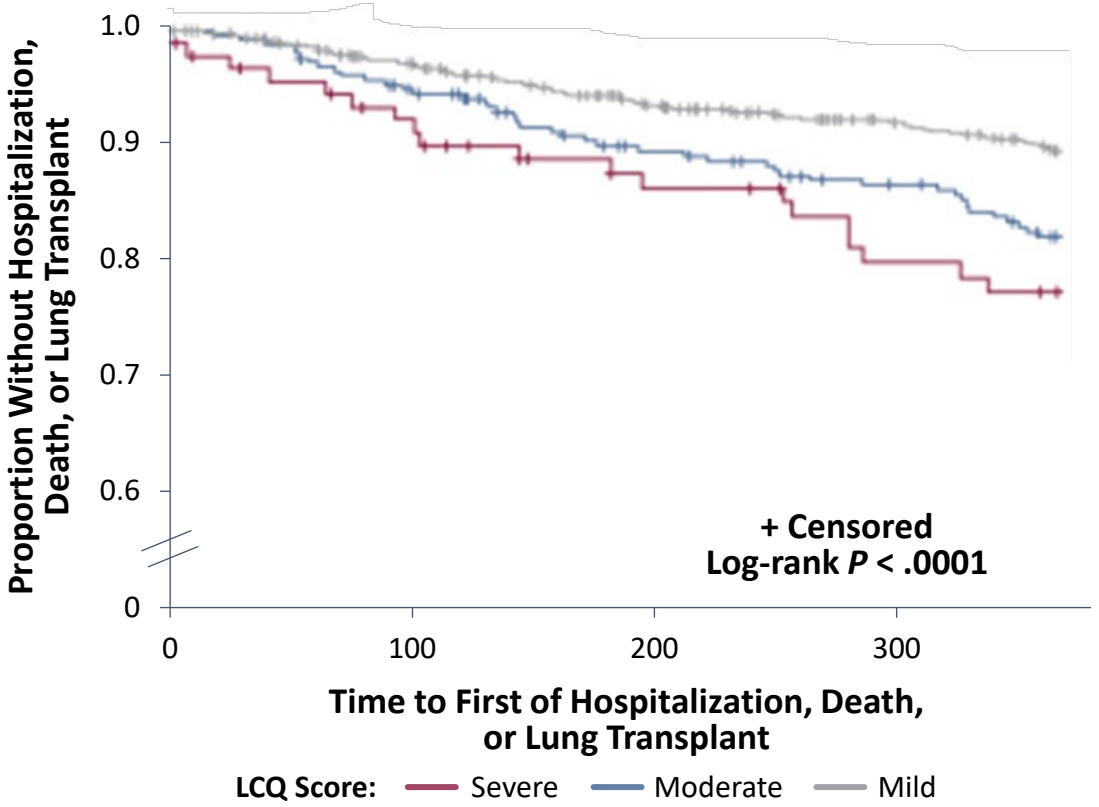
Patients with Idiopathic Pulmonary Fibrosis (IPF) and non-IPF Interstitial Lung Disease-Related (non-IPF ILD) Chronic Cough



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

- No FDA approved therapies in the US
- 150k US patients with IPF[1-3]
- 60-70% of IPF patients have uncontrolled chronic cough[4]
- 3-5 year median life expectancy[5]
- Cough's role in IPF/ILDs[6-9]:
  - A higher cough severity 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 from the US Pulmonary Fibrosis Foundation Registry (N=1,447)

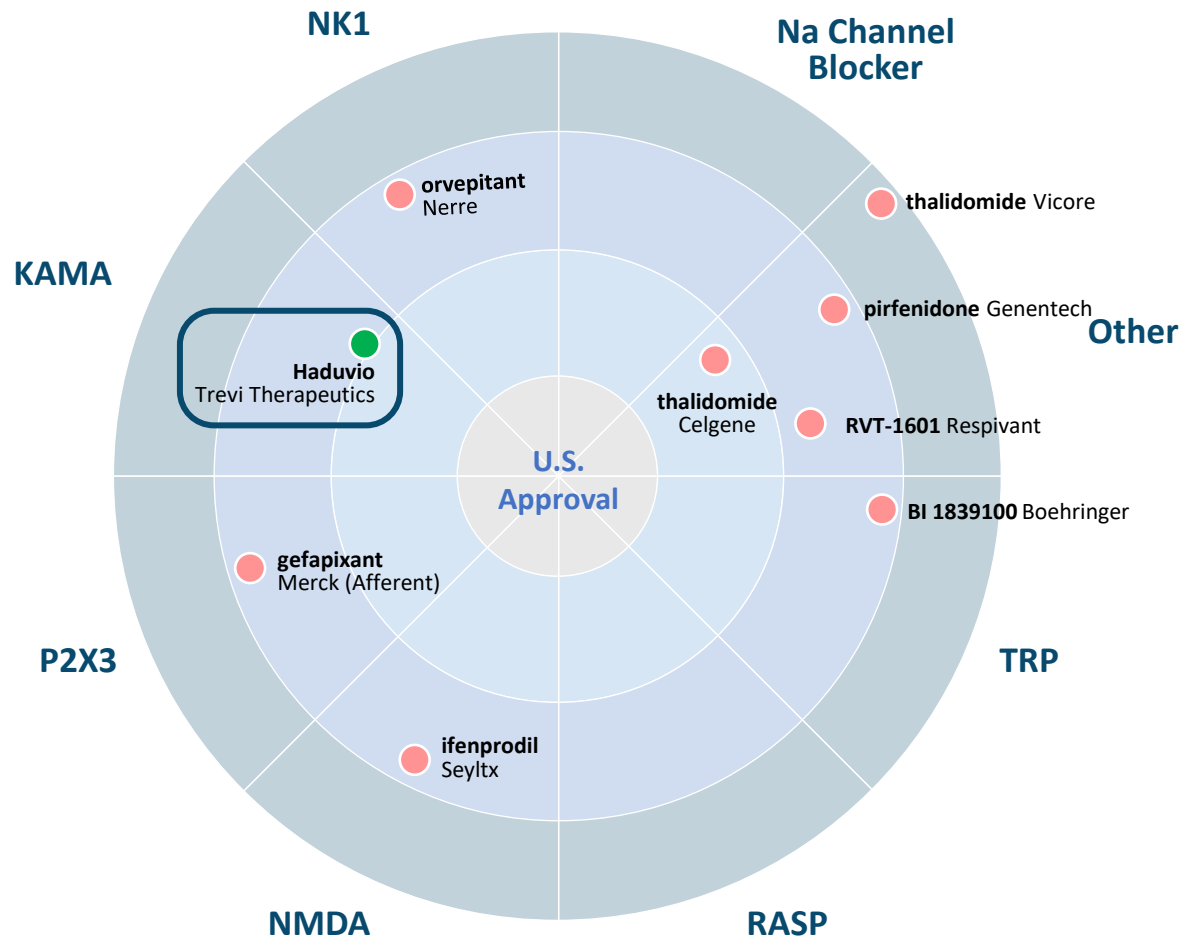


[1]Raghu G et al. ERJ 2016 doi: 10.1183/13993003.01653-2015 [2]Raghu G et al. Lancet Respir Med 2014 doi: 10.1016/S2213-2600(14)70101-8 [3]U.S. Census NC-EST2023-AGESEX-RES [4]Interviews and quantitative study conducted by Indegene for Trevi, June 2022 with US pulmonologists (n = 100) [5]Raghu G et al. 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 Only Mechanisms Have Failed in IPF-Related Chronic Cough

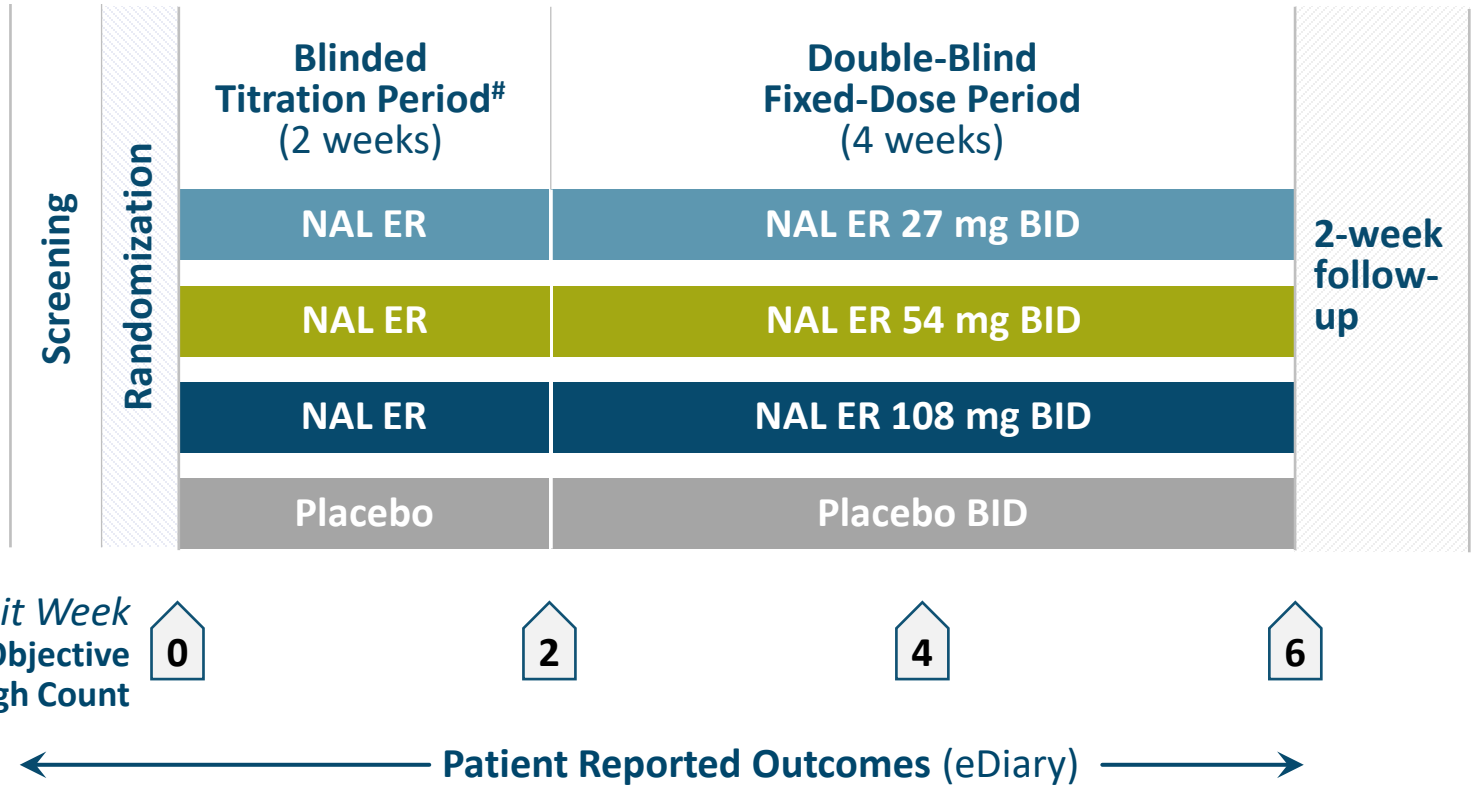
- P2x3: gefapixant
- TRPA1: BI 1839100
- NK1: orvepitant

Anti-Fibrotics Have Not Shown Cough Benefit

- Aim to slow the progression of the disease
- No objective or patient-reported outcome cough benefit in clinical trials

Sources: Haduvio, Trevi Therapeutics: DOI: 10.1056/EVIDoa2300083, Orvepitant, Nerre: clinicaltrials.gov/study/NCT05185089, Gefapixant, Merck: doi: 10.1007/s41030-021-00162-9, Ifenprodil, Algernon: Algernon Pharmaceuticals Press Release January 9, 2023, Ifenprodil, Algernon: 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



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)
- E-RS:IPF®, LCQ, L-IPF, EQ-5D-5L
- PGI-S, PGI-C Cough, PGI-S, PGI-C IPF
- CGI-C, CGI-S Cough

Objective Cough Monitor

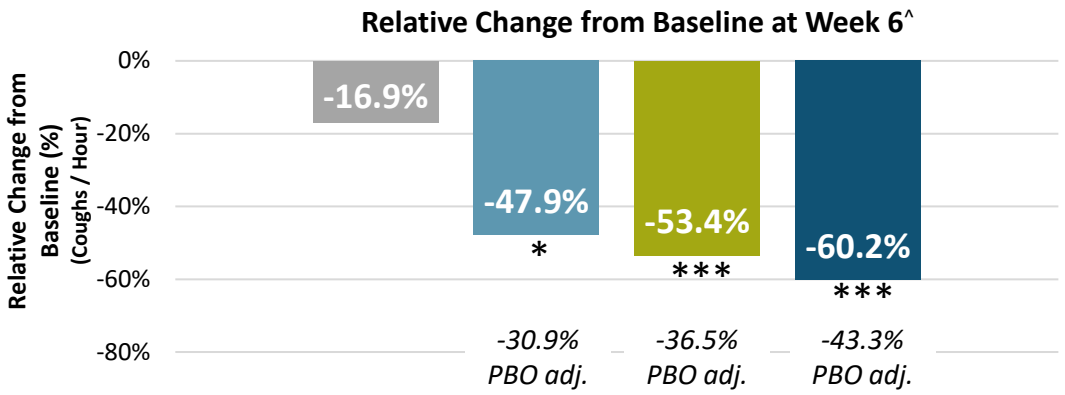
VitaloJAK® Cough Monitor

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)

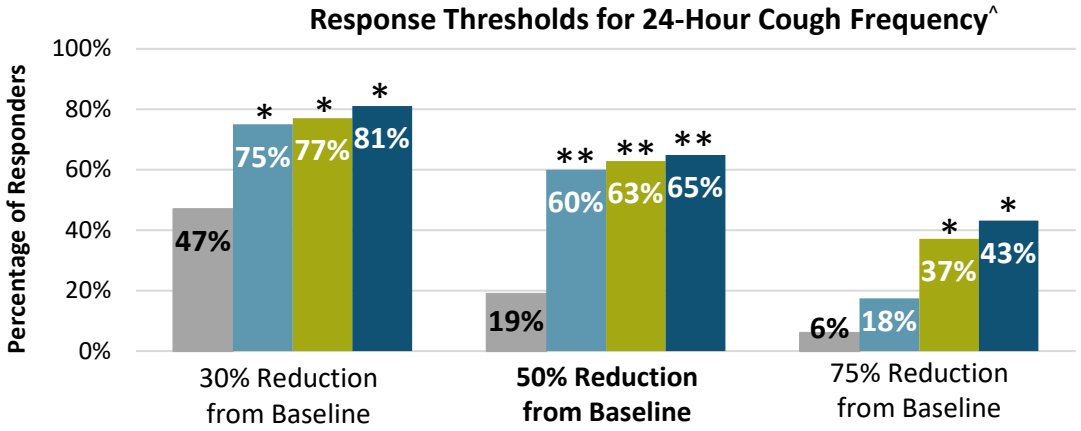
Selected data included in topline results
NAL ER / nalbuphine ER is an investigational therapy
E-RS:IPF: Exacerbation of Chronic Pulmonary Disease Tool IPF, CS-NRS: Cough Severity Numerical Rating Scale, LCQ: Leicester cough questionnaire, L-IPF: Living with IPF, EQ-5D-5L: EuroQoL 5-Dimension 5-Level, 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
Clinicaltrials.gov ID: NCT05964335

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

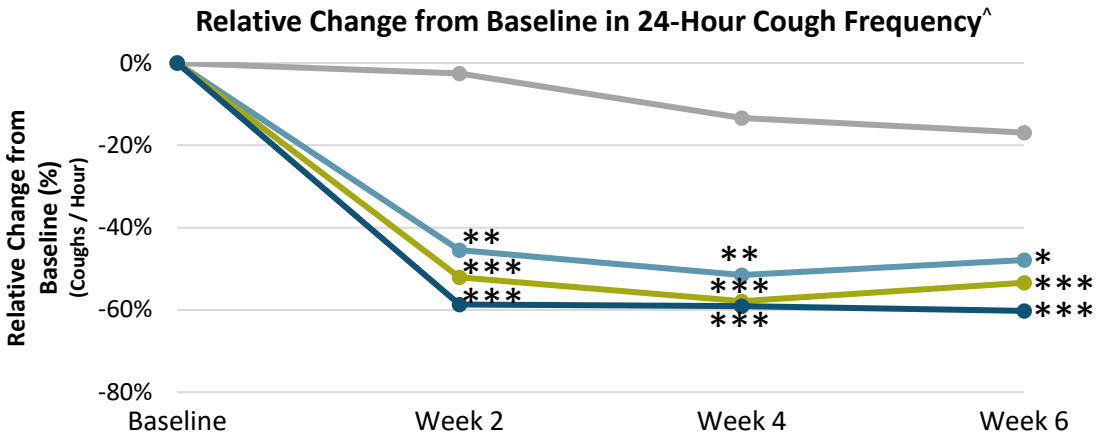
Significant Reduction in Cough Frequency (Primary Endpoint)



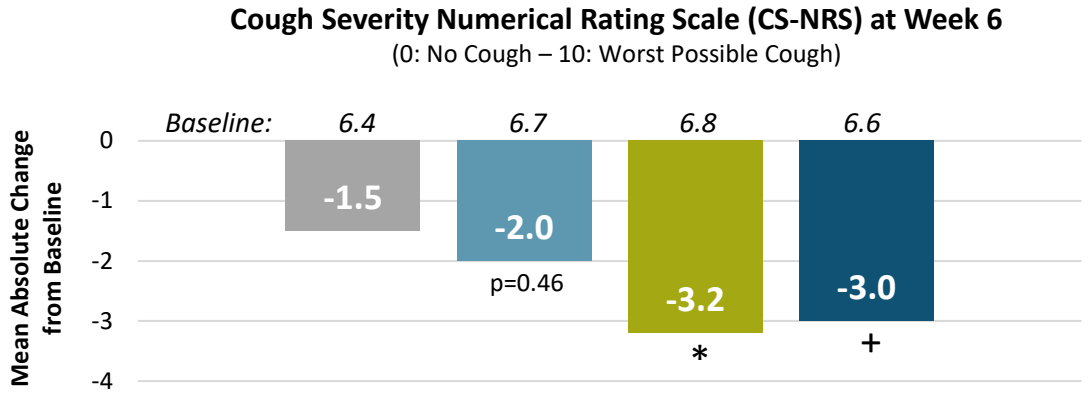
Broad Coverage Clinically Meaningful Response



Rapid and Persistent Cough Reduction



Significant Reduction in Patient-Reported Outcomes with 54 mg BID



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

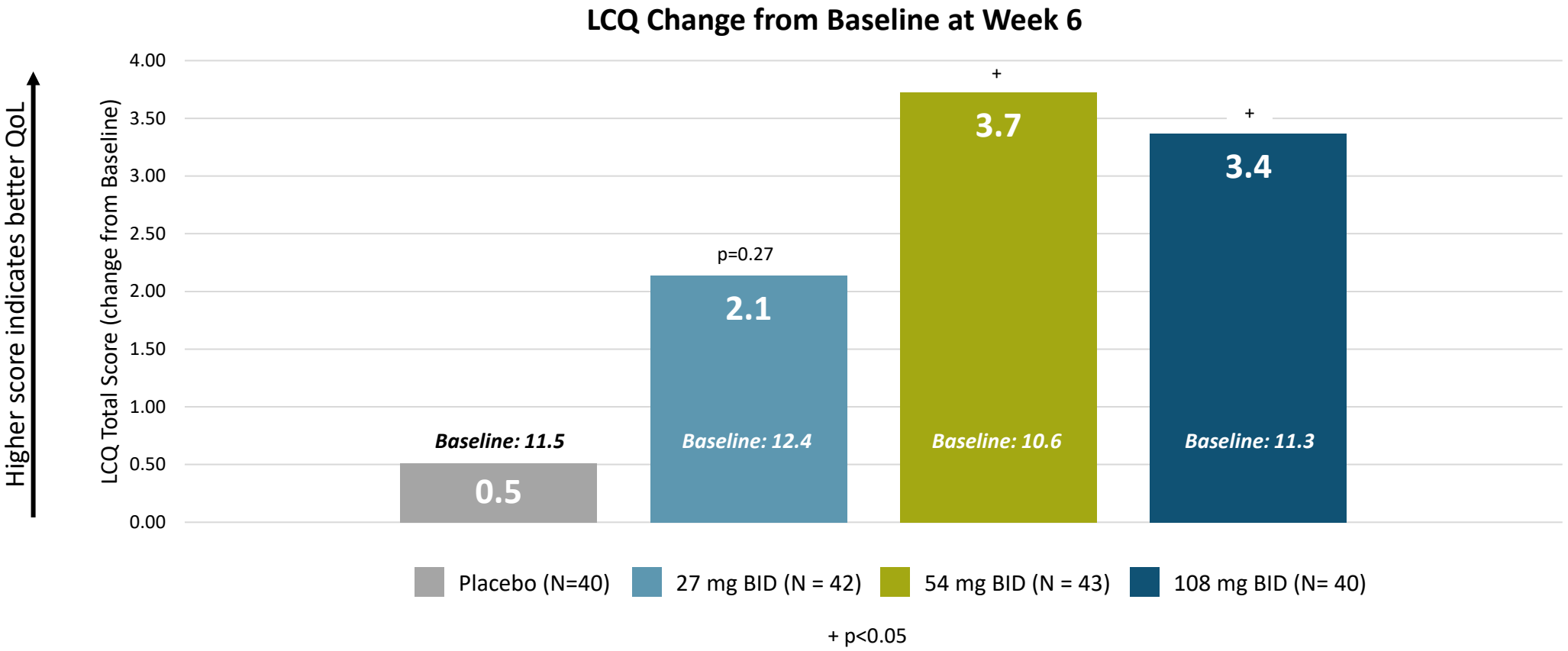
NAL ER / nalbuphine ER is an investigational therapy
mITT population, Primary efficacy analysis conducted on log-transformed cough frequency data
^One placebo patient with an extreme outlier value at Week 6 was excluded from the modified intent-to-treat (mITT) population. Inclusion of the patient in 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 those subjects meeting the pre-specified threshold
[1]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

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)

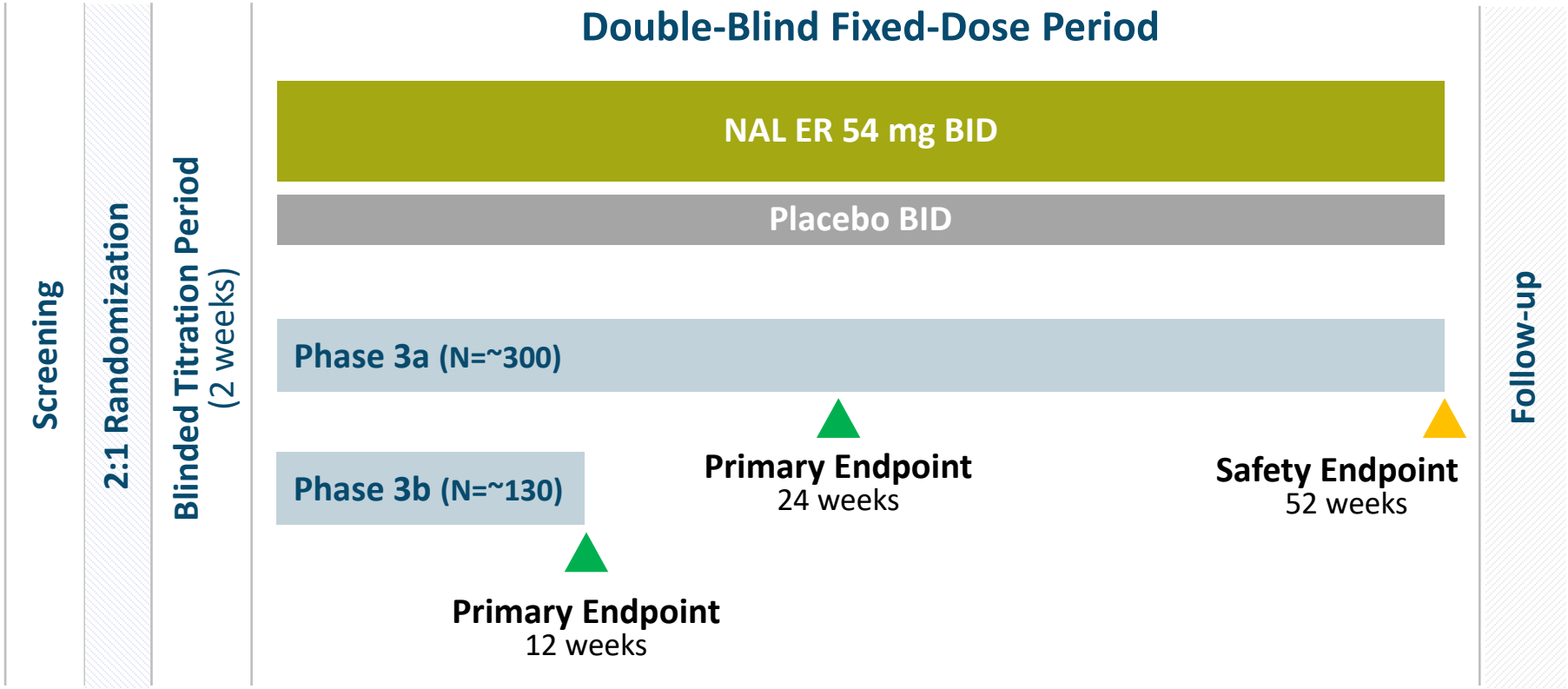
Post-hoc analysis to determine onset of adverse event by actual dose received

- 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%)

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

Phase 3 Clinical Trial Designs in Patients with IPF-Related Chronic Cough

Two Phase 3 randomized, double-blind, placebo-controlled, multicenter, global trials



Primary Efficacy Endpoint

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

Key Secondary Endpoint

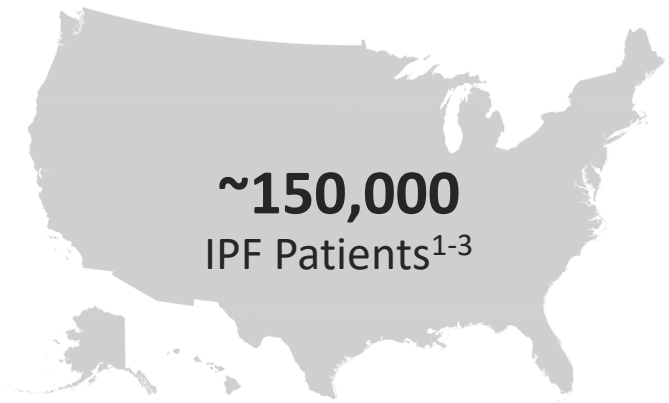
- Relative change from Baseline in Cough Severity Numerical Rating Scale (CS-NRS)

Initiation Expected for Phase 3a 2Q 2026 and Phase 3b 2H 2026

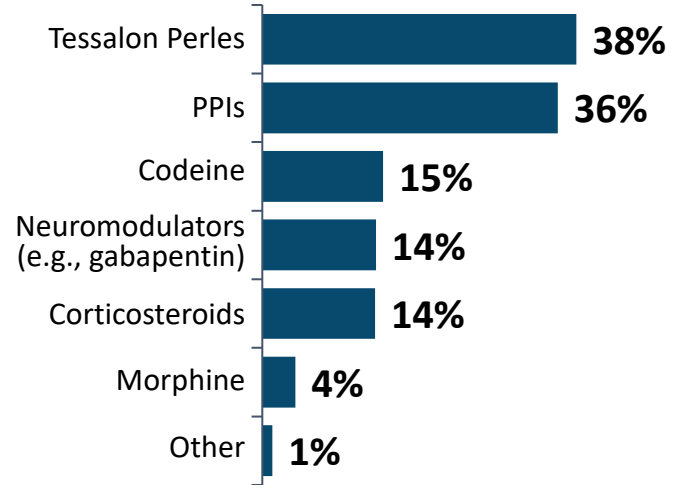
Trial designs are subject to final review of the protocol by the FDA.
Development plans reflect FDA feedback from the End of Phase II Meeting.
NAL ER / nalbuphine ER is an investigational therapy

$2-3B Haduvio Opportunity in IPF Leading with a Specialty Indication with a High Unmet Need and Favorable Commercial Dynamics

US IPF Opportunity Today

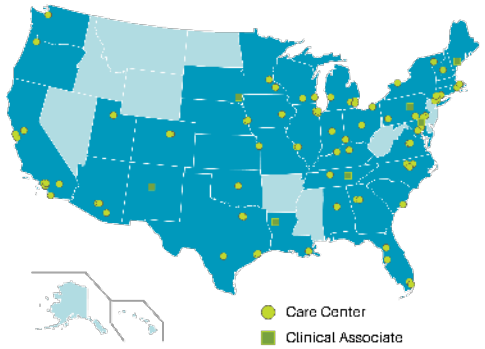


IPF Cough Treatment Paradigm[4]



Expected Commercial Model

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



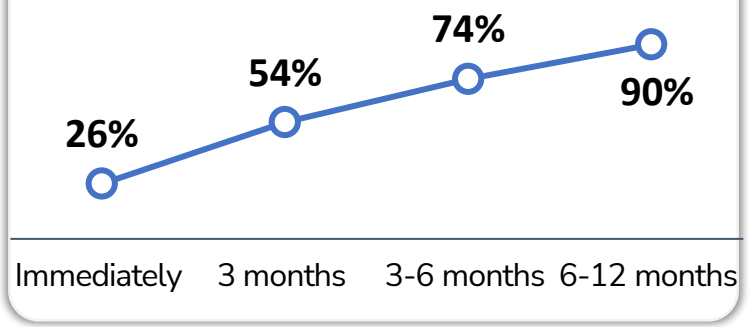
60-70%

Avg. % of IPF patients with uncontrolled chronic cough

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

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

Rapid Potential Prescribing Uptake[4]



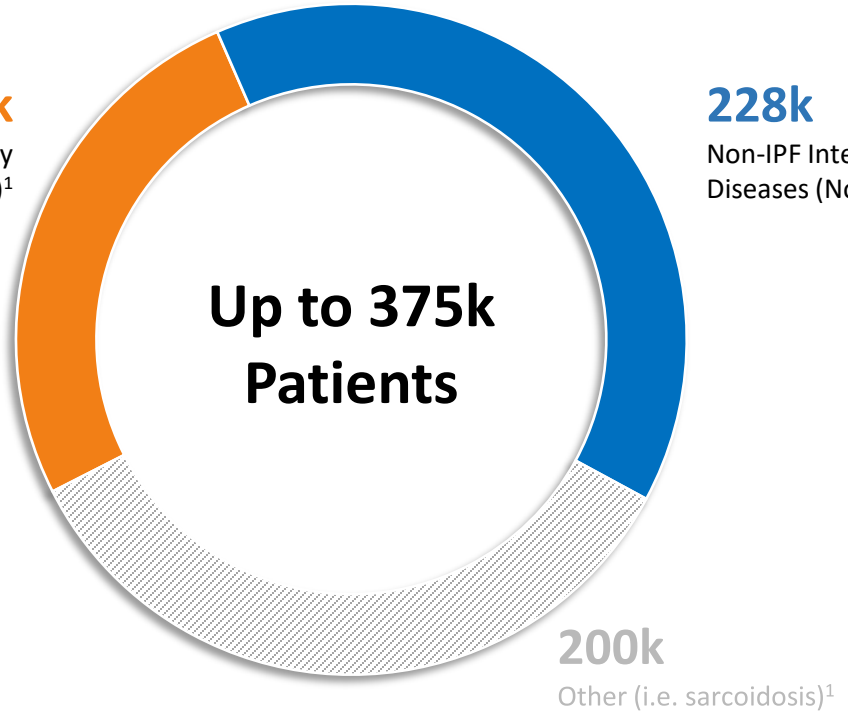
YoY: Year-on-year, PPI: proton-pump inhibitors

[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]Interviews and quantitative study conducted by Indegene for Trevi, June 2022 with US pulmonologists (n = 100) [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

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

$2-3B Haduvio Expansion Opportunity Into Patients with Non-IPF ILD-Related Chronic Cough

Estimated 2025 US ILD Prevalence



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[2,3]

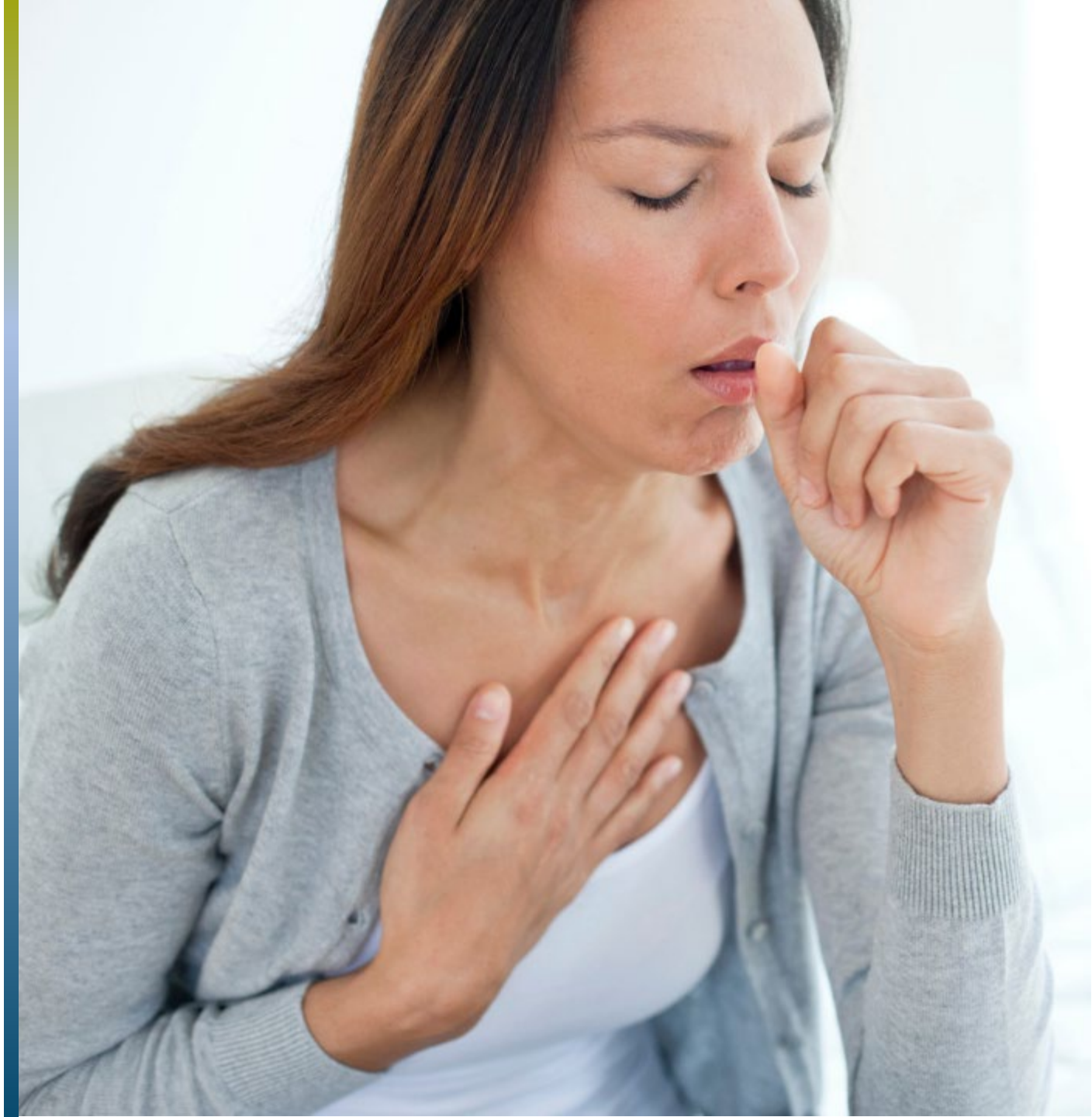
- Underlying lung fibrosis
- 50-60% have uncontrolled chronic cough
- No approved therapies for chronic cough
- High negative impact on QoL

Next Steps

- Complete draft protocol
- Meet with the FDA

[1]Trevi Internal Analysis [2]No approved therapies in the US for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC [3]Based on survey conducted by Trevi Therapeutics, April 2025 [3]Based on Pulmonologists who managed Non-IPF PF-ILD patients with chronic cough in the last 12 months, June 2022 (N=30)
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

Patients with Refractory Chronic Cough (RCC)



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

Average of 8 years with chronic cough prior to diagnosis

61% have anxiety and/or depression

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

Impaired physical and psychological health

No FDA-approved therapies

River Patient

60 year-old male
Chronic cough since 1977 (>45 years)

Tried two cough therapies and codeine

<u>24-hour cough frequency</u>
Baseline: 49.58 coughs/hour (1,190/day)

-90% on NAL ER

+3% on Placebo

<u>Cough Severity-VAS (CS-VAS)</u>

-63% (-41 mm) on NAL ER

-14% (-12 mm) on Placebo

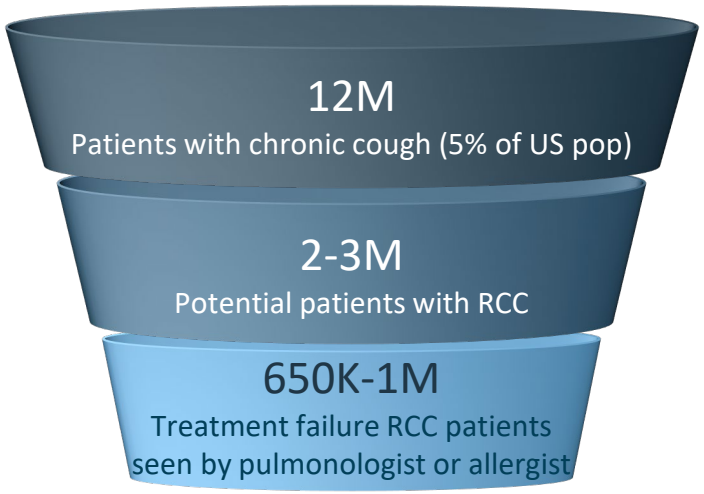
Change from Baseline at Day 21

Selected patient in the RIVER trial and not necessarily representative of the trial population as a whole

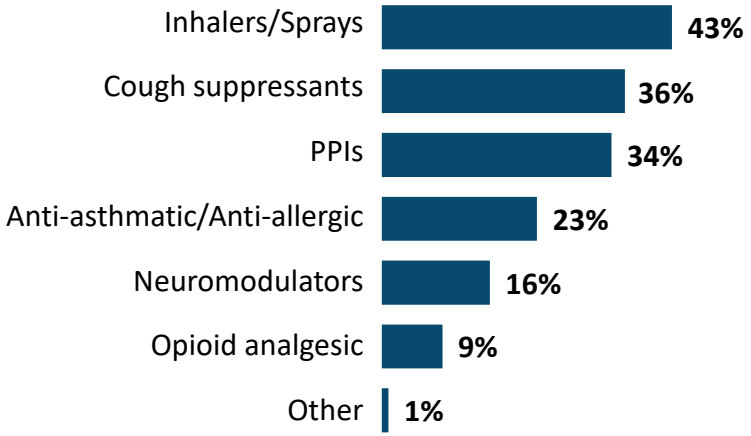
Sources: Smith JA et al, Respir Res 2024 doi.org/10.1186/s12931-024-02881-4, Puente-Maestu L et al, ERJ Open Res 2023 doi.org/10.1183/23120541.00425-2023, Gibson P et al, Chest 2016 doi:10.1378/chest.15-1496, Brister D et al. Lung 2024 DOI: 10.1007/s00408-024-00714-1
NAL ER / nalbuphine ER is an investigational therapy

A Specialty Commercial Model in the RCC Market

US RCC Opportunity

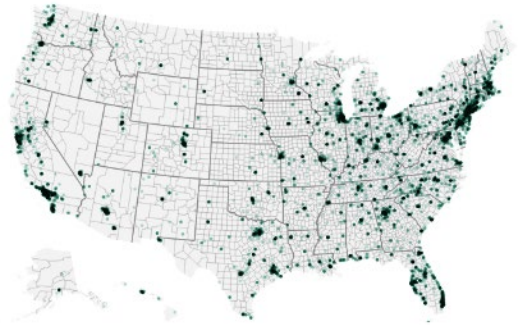


Current Treatment Paradigm



RCC Commercial Model

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



Focus on treatment failures:

- **High unmet need**
- **RCC patients failing earlier lines of therapy**
- **Maintains specialty pricing across IPF and RCC**

No FDA-approved therapies

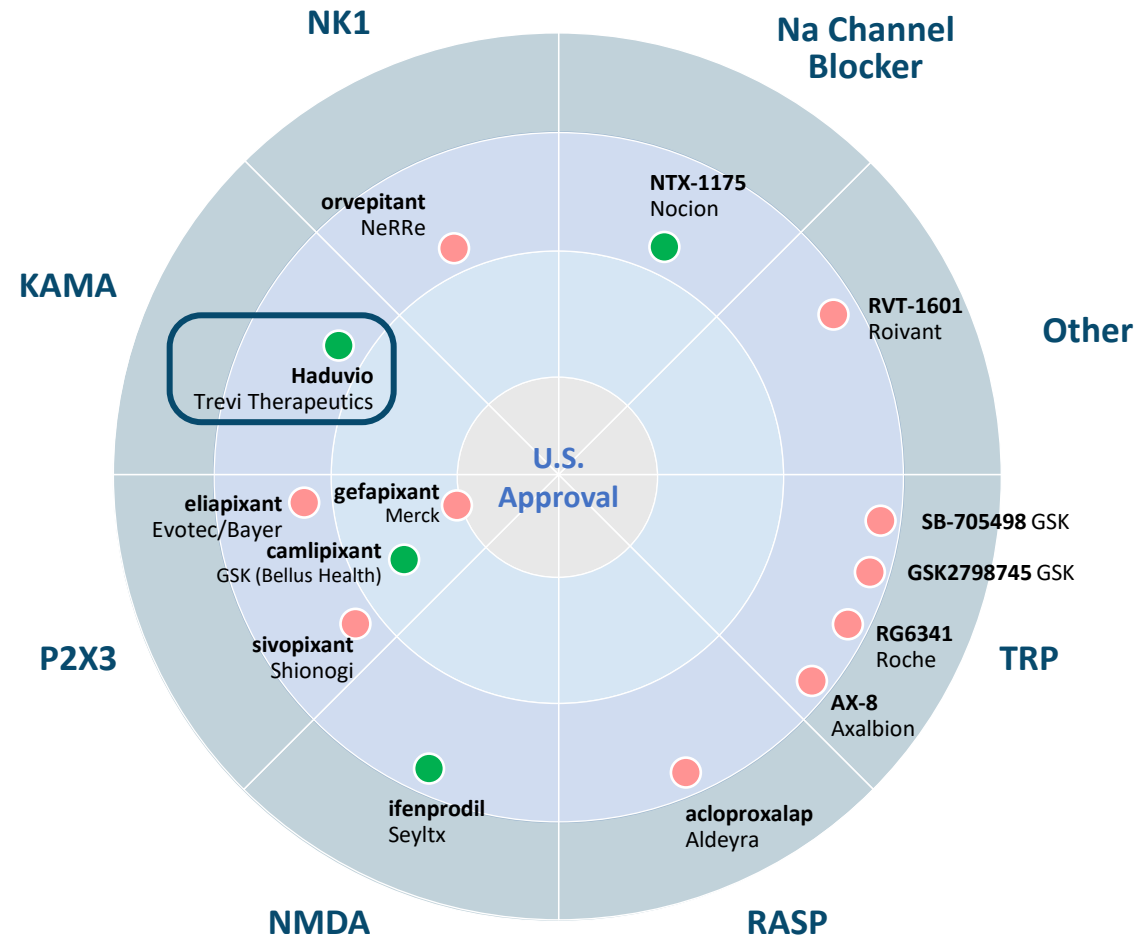
High unmet need (5.8 / 7) and dissatisfaction (4.5 / 7) with current therapies

~1/3 RCC patients see a pulmonologist or allergist

Efficient proposed sales model with IPF/ILD (~10 incremental reps expected)

RCC Opportunity: DOI: 10.1016/j.jaip.2021.07.022, DOI: 10.1177/00368504241238080, LifeSci Patient Survey 2022 (N=1,000)
RCC Current Treatments: Interviews and quantitative study conducted by Indegene, 2024 with US physicians (n = 152)
Pulmonologist map: HealthLink Dimensions data
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy

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

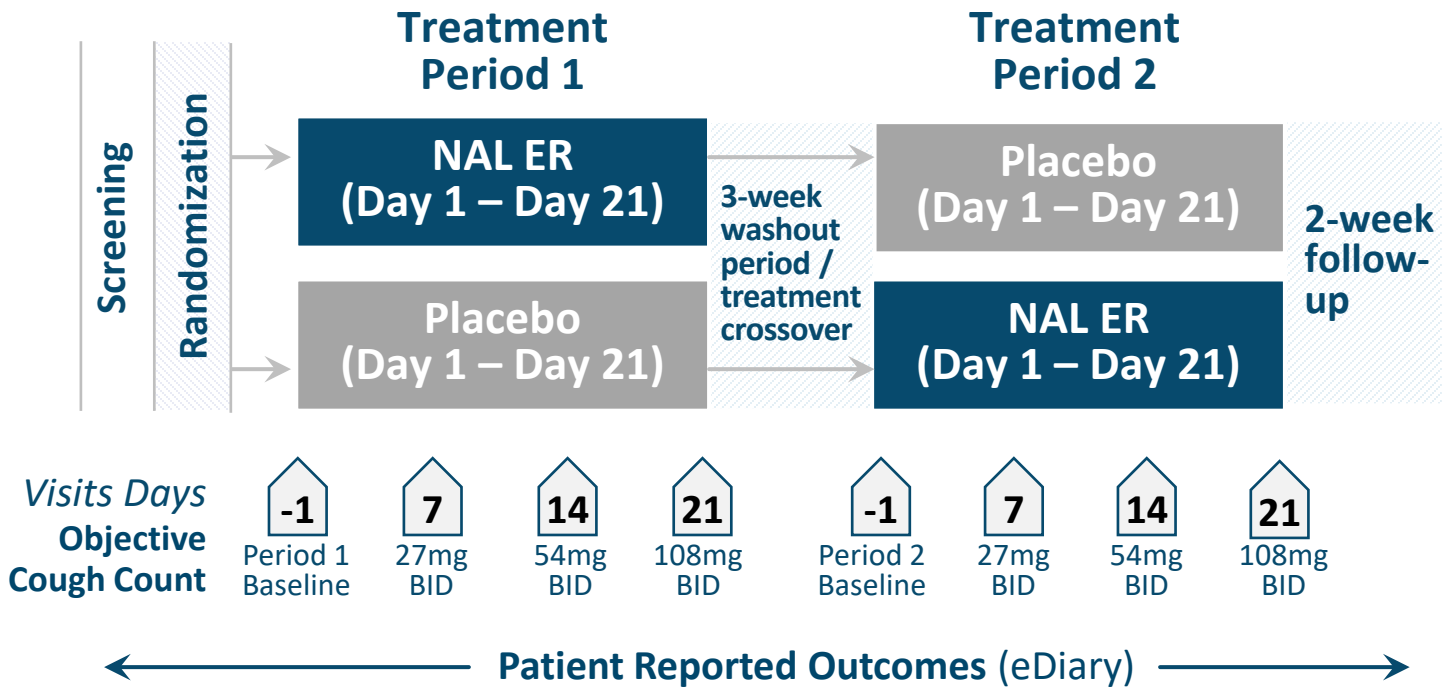


Haduvio is well-positioned in a category with a high unmet need and no FDA-approved therapies

- 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, GSK: doi: 10.1016/j.jaci.2014.01.038, GSK2798745, GSK: doi: 10.1183/23120541.00269-2021, RG6341, Roche: Roche YTD September 2024 Sales Presentation, AX-8, Axalbion: Axalbion Press Release August 27, 2024, 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

RIVER Phase 2a Clinical Trial in RCC



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

Primary Efficacy Endpoint

- 24-hour cough frequency using objective cough monitor

Secondary Endpoints

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

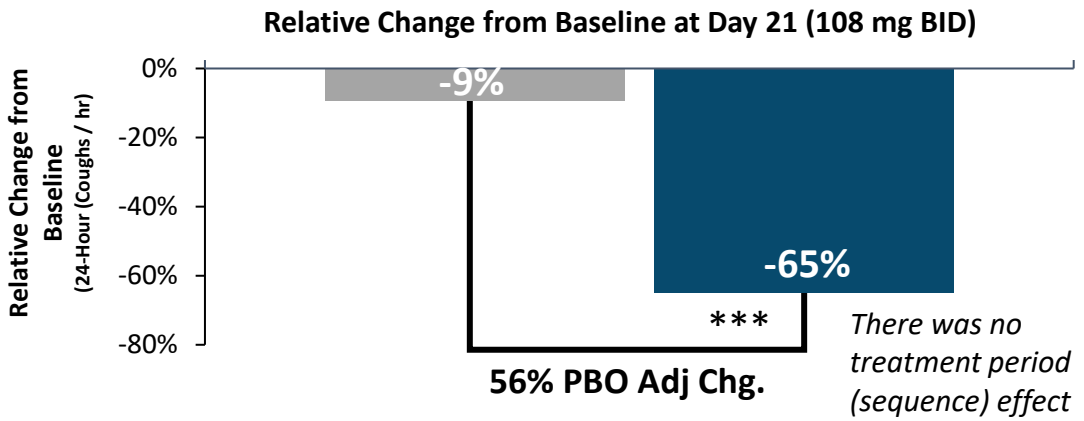
Objective Cough Monitor

VitaloJAK® Cough Monitor

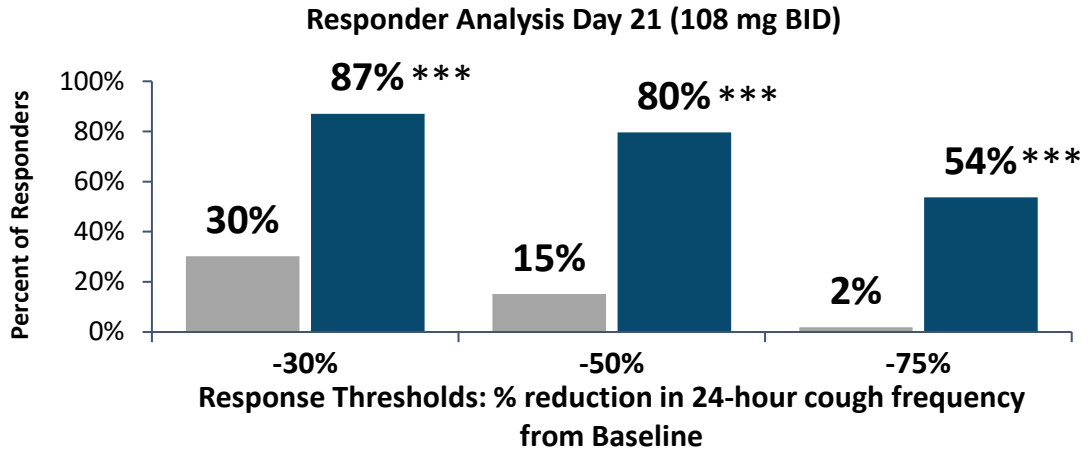
Selected data included in topline results
BID: twice daily, CS-VAS: cough severity visual analog scale, LCQ: Leicester cough questionnaire, PGI-S: patient global impression of cough severity, PGI-C: patient global impression of change in cough, CGI-S: clinician global impression of cough severity, CGI-C: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

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

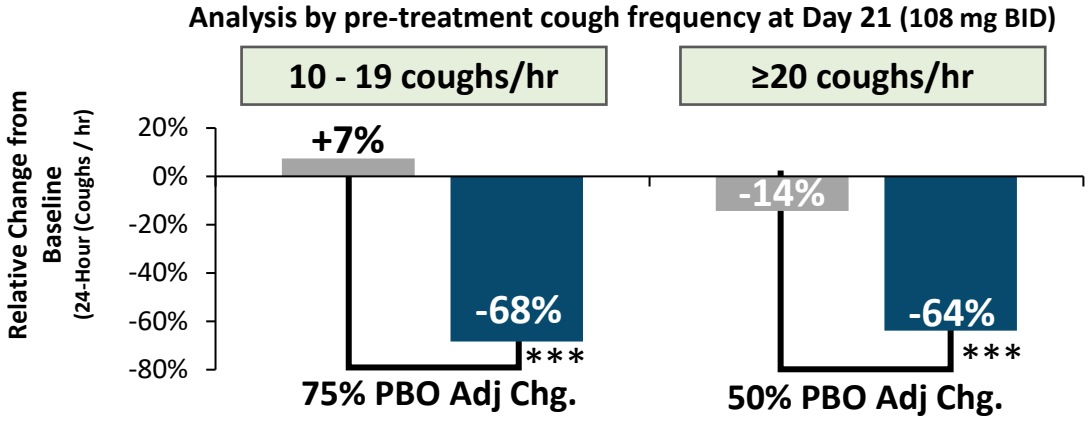
Significant Reduction in Cough Frequency (Primary Endpoint)



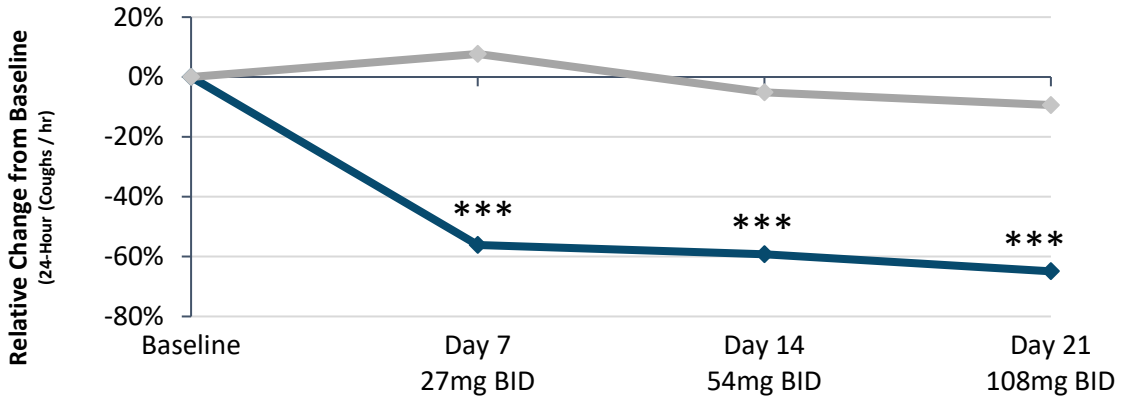
Broad Coverage Clinically Meaningful Response



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

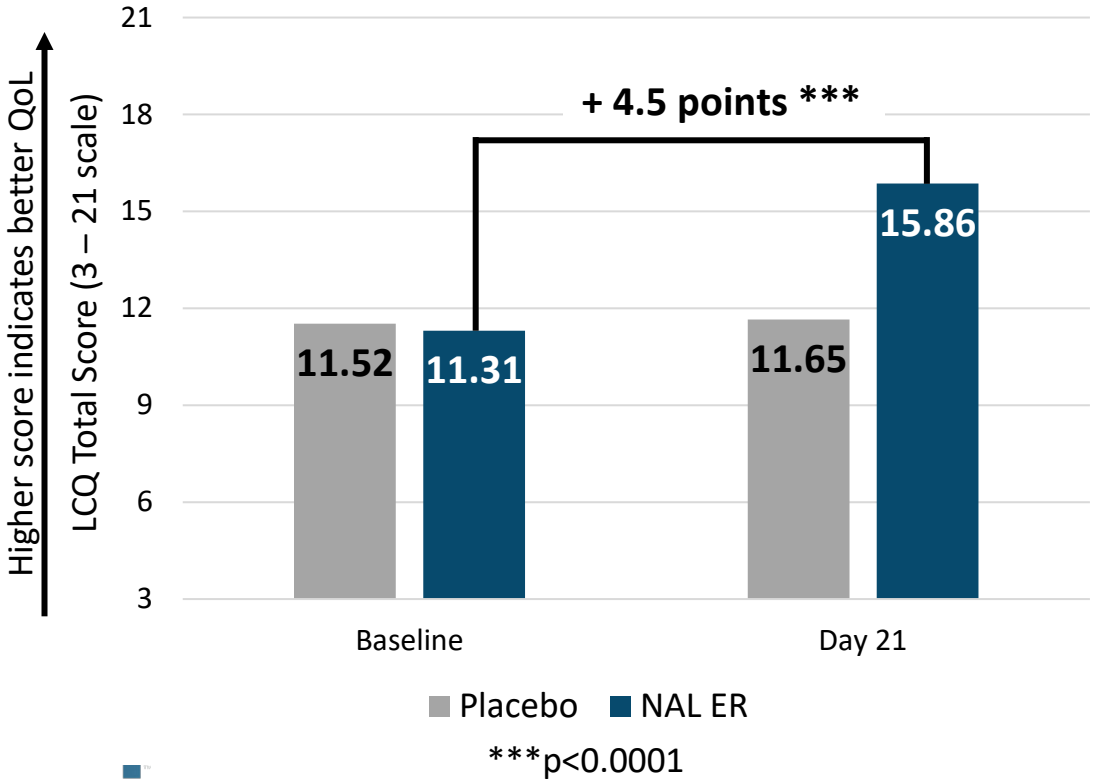
Primary efficacy analysis conducted on log-transformed cough frequency data
NAL ER / nalbuphine ER is an investigational therapy
All graphs: Change from Baseline, Responder Analysis and Rapid Onset all conducted on the FAS population.

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

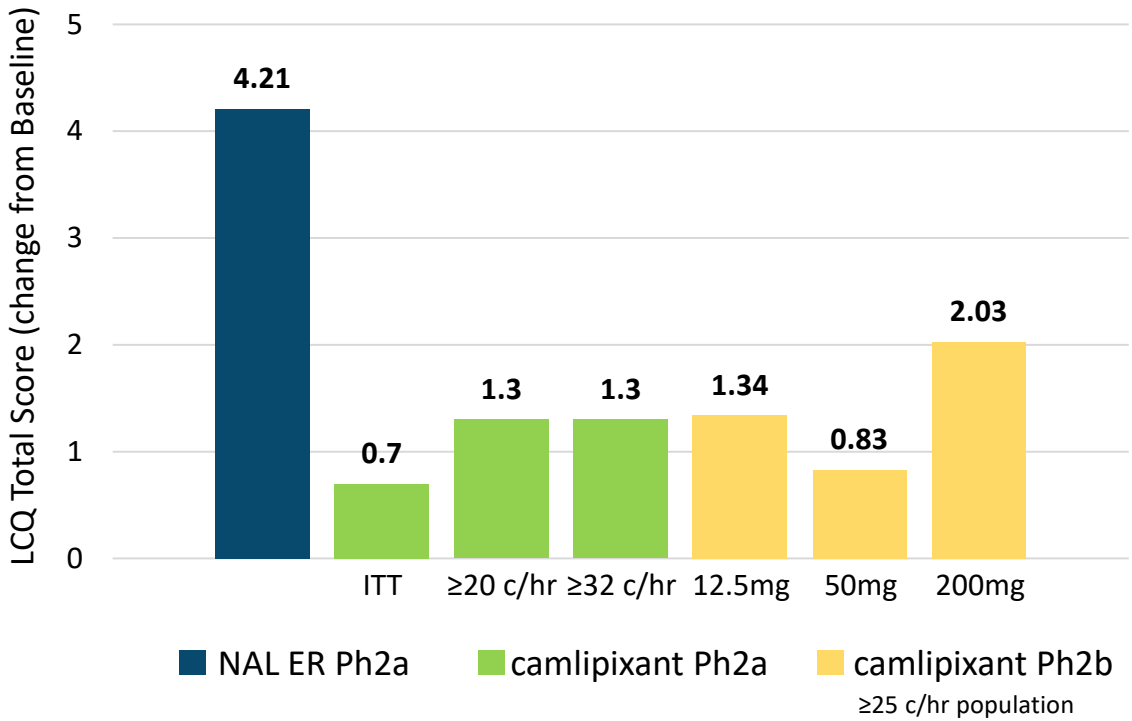
NAL ER LCQ Total Score



***p<0.0001

LCQ Total Score Placebo Adjusted Change

NAL ER comparison to camlipixant



≥25 c/hr population

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

LCQ: Leichester Cough Questionnaire

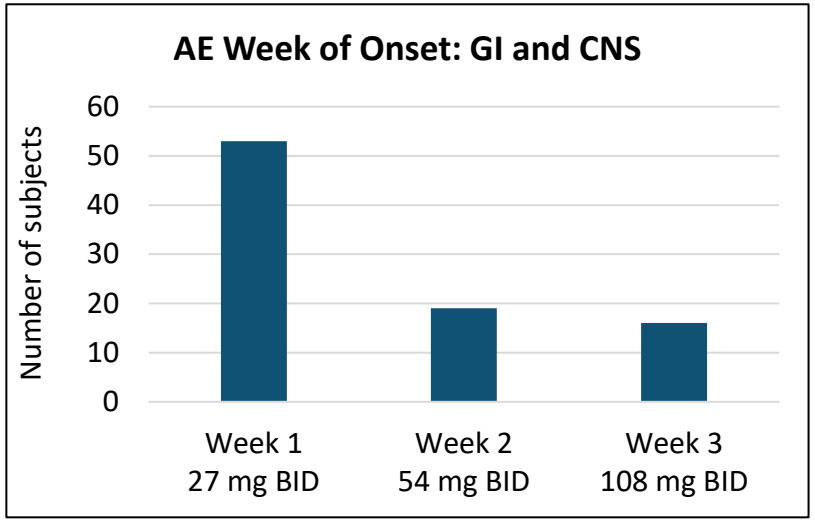
NAL ER / nalbuphine ER is an investigational therapy

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)

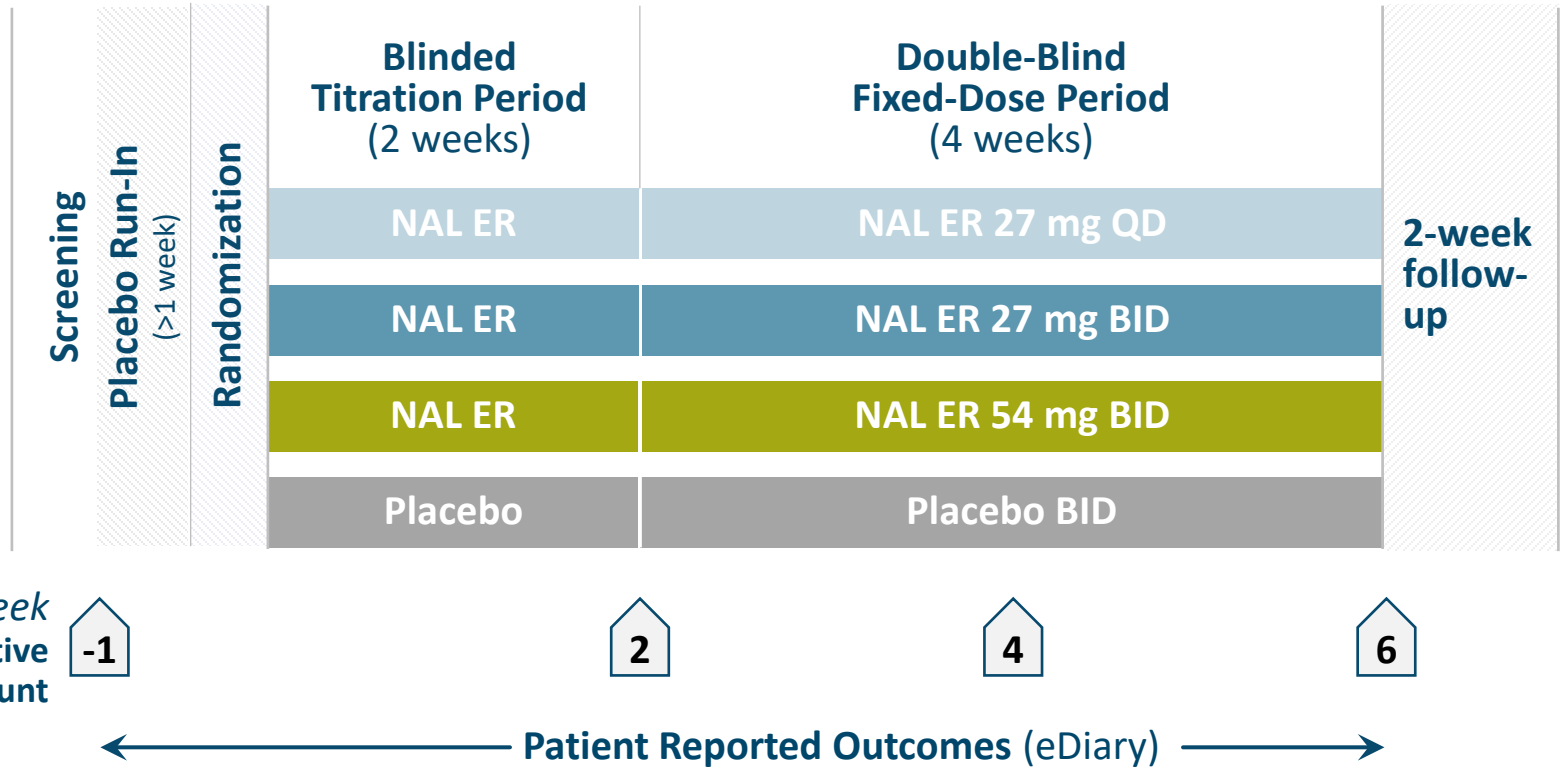
There were no treatment emergent serious adverse events
Six patients experienced treatment-emergent AEs that were CTCAE Grade 3:
NAL ER (4 patients): Somnolence, dizziness, headache, hypoaesthesia, lethargy, nephrolithiasis
Placebo (2 patients): Headache and blepharitis
There were no CTCAE treatment-emergent 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
NAL ER / nalbuphine ER is an investigational therapy
Subject is included only once, even if they experienced multiple events in that preferred term

Phase 2b Clinical Trial Design in RCC (N ~100)



24-hour cough frequency inclusion criteria:
≥10 coughs/hour

Primary Efficacy Endpoint

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

Secondary Endpoints

- Chronic cough patient reported outcomes

Objective Cough Monitor

VitaloJAK® Cough Monitor

Initiation Expected 2Q 2026

NAL ER / nalbuphine ER is an investigational therapy

Milestones and Value Creation

First Half 2026

Expected Clinical Development Milestones

- ✓ Completed End-of-Phase 2 Meeting with the FDA for IPF-related Chronic Cough Program
- Initiation of the Phase 2b RCC trial
- Initiation of Phase 3a IPF-related chronic cough trial

Clinical Trial Data Visibility

- ✓ CORAL data published in JAMA
- New data presentations at the American Thoracic Society's (ATS) 2026 International Conference

Second Half 2026

Expected Clinical Development Milestones

- Initiation of Phase 3b IPF-related chronic cough trial
- Initiation of the non-IPF ILD-related chronic cough trial
- Enrollment updates in IPF-related chronic cough and RCC

Clinical Trial Data Visibility

- European Respiratory Society (ERS) Congress 2026
- CHEST Annual Meeting

$188.3M in cash, cash equivalents and marketable securities as of 12/31/25

Estimated cash runway into 2028

trevi THERAPEUTICS

Development plans subject to discussions with regulatory authorities
Haduvio (NAL ER / nalbuphine ER) is an investigational therapy