Corporate Presentation

March 2024

Nasdaq: TRVI

Forward Looking Statement Disclaimer

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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.

Haduvio Advancing Clinical Development Plans

Haduvio (nalbuphine ER)

Indications	Preclinical	Phase 1	Phase 2	Phase 3
Chronic Cough in Idiopathic Pulmonary Fibrosis (IPF)			●	
Refractory Chronic Cough (RCC)			●	

Supporting Clinical Studies

- Ph1b Respiratory Physiology Study in IPF
- Human Abuse Potential (HAP) Study

CANAL

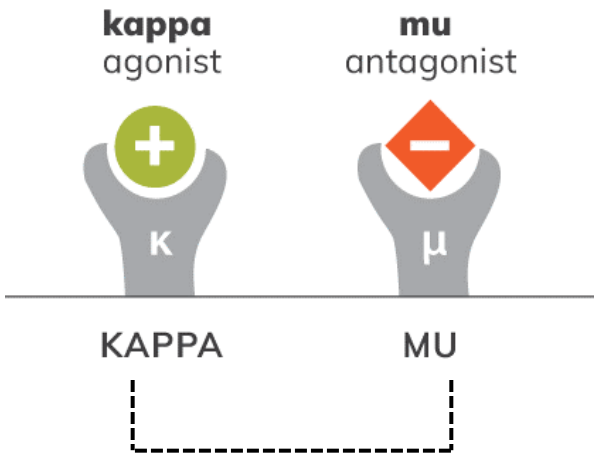
Ph2a Data Supports Mechanism in IPF Chronic Cough

- 75.1% reduction in daytime cough frequency from study baseline, 52.5% placebo-adjusted change ($p<0.0001$)
- Patient and clinician reported outcomes were consistent with the reduction in daytime cough frequency and were statistically significant

Haduvio™ (nalbuphine ER) Has Multiple Applications in Chronic Cough Due to a Novel Mechanism of Action and Both Central and Peripheral Activity

Novel Dual-Acting Mechanism of Action

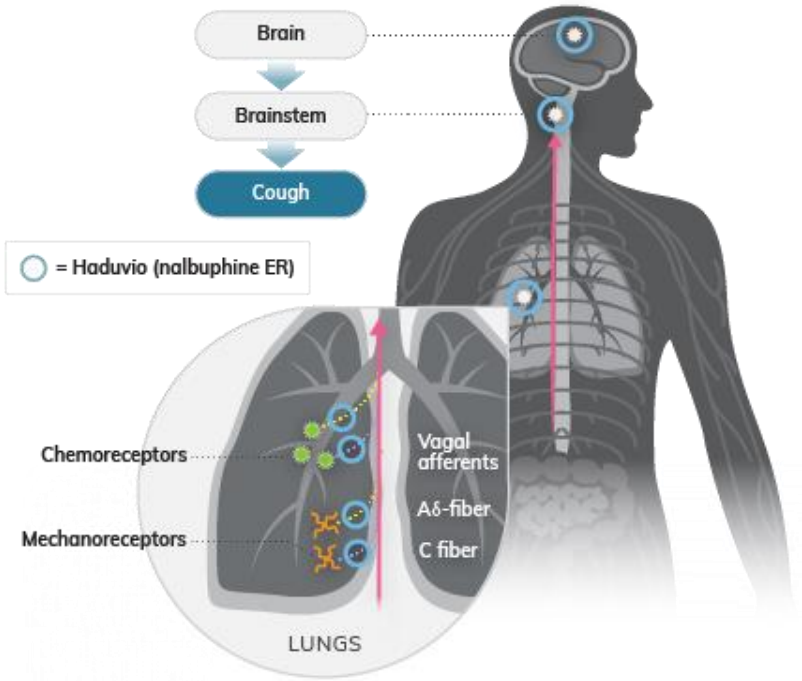
Kappa agonists and mu antagonists work across the neuroinflammatory axis to rebalance hypersensitivity conditions, such as chronic cough



Dynamic interchange between the two receptors

Importance of Central and Peripheral Activity

Synergistically works both centrally in the brain and peripherally in the lungs to provide an anti-tussive effect independent of the peripheral cough stimuli



Graphic: Vigeland CL et al, Respiratory Medicine 2017 doi.org/10.1016/j.rmed.2016.12.016

Haduvio™ Has a Well-Characterized Efficacy, Safety, and Durability Profile

Demonstrated Efficacy Across Indications

- ☑ Largest absolute reduction in cough frequency (75%) and placebo-adjusted change (52%) in chronic cough
- ☑ Only successful trial in IPF chronic cough (p<0.0001)
- ☑ Significant Ph2b/3 prurigo nodularis trial (p=0.0157)
- ☑ Significant Ph2b/3 uremic pruritus trial (p=0.017)

Robust Clinical Experience

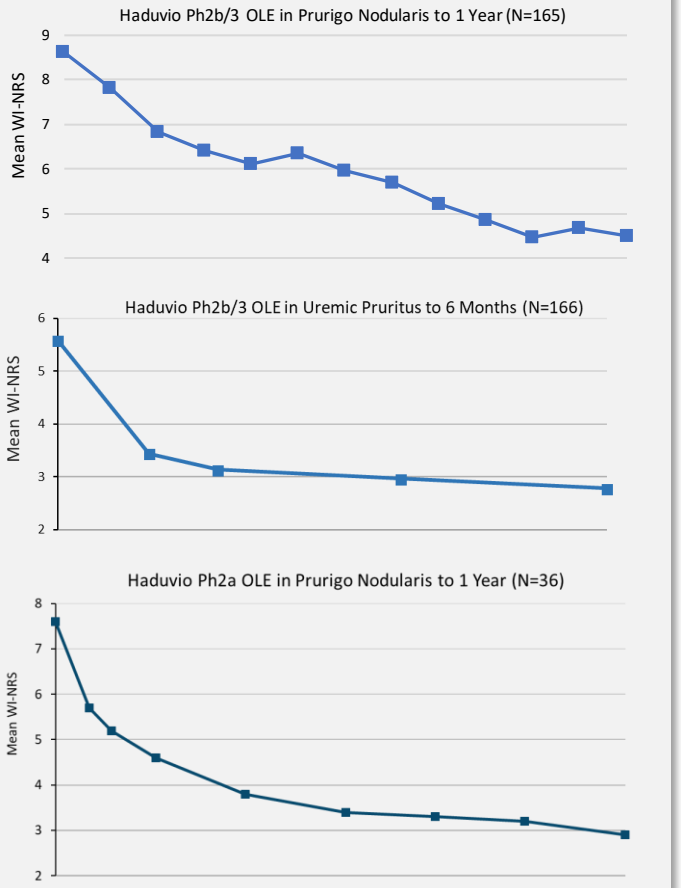
1,140 total subjects dosed

273 subjects dosed to 6 months

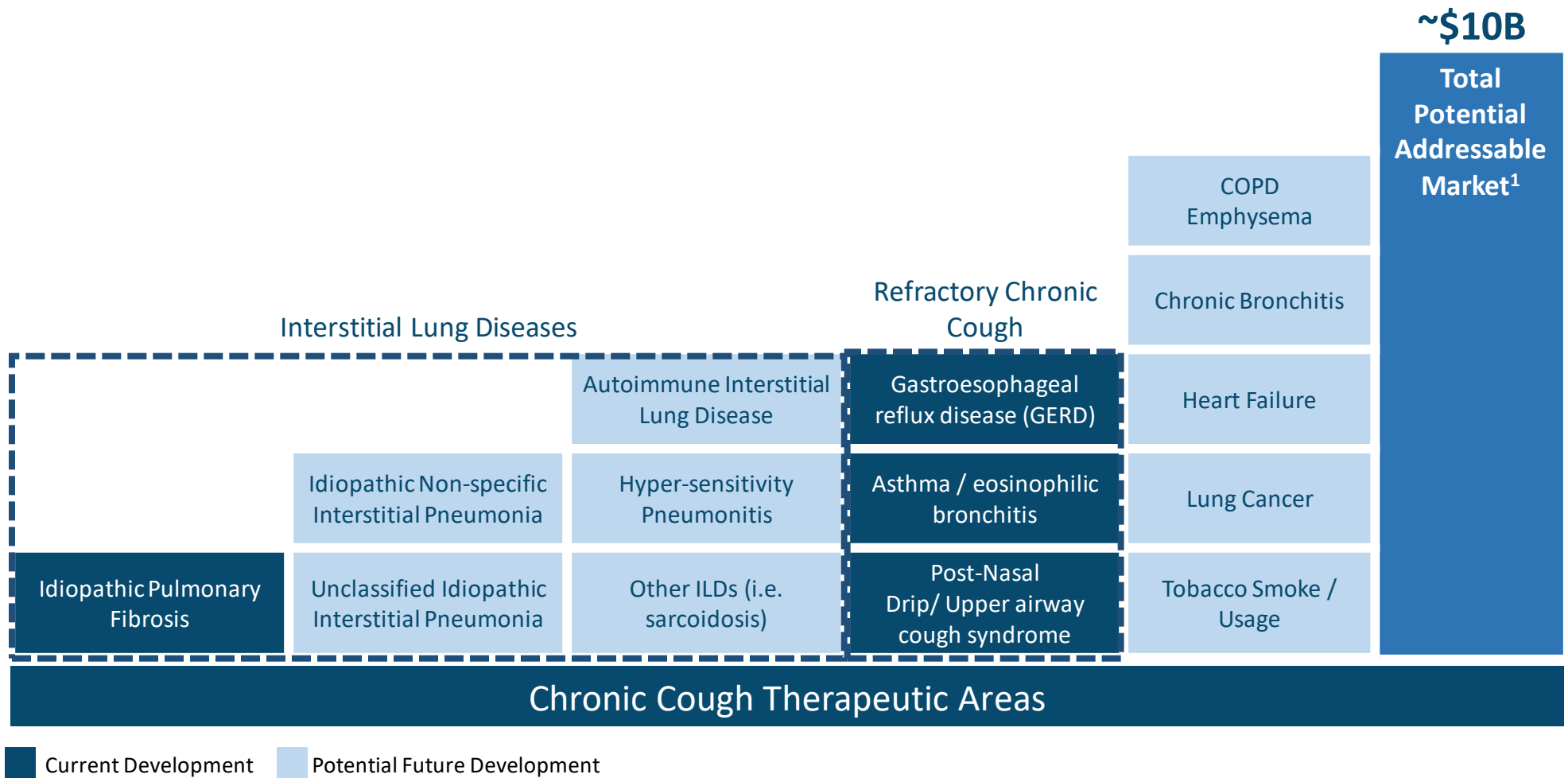
87 subjects dosed to 1 year

Haduvio studied in a **range of severe chronic conditions** (IPF, hepatic impairment, renal impairment)

Durable Effect Up to 1 Year



Opportunities in Chronic Cough



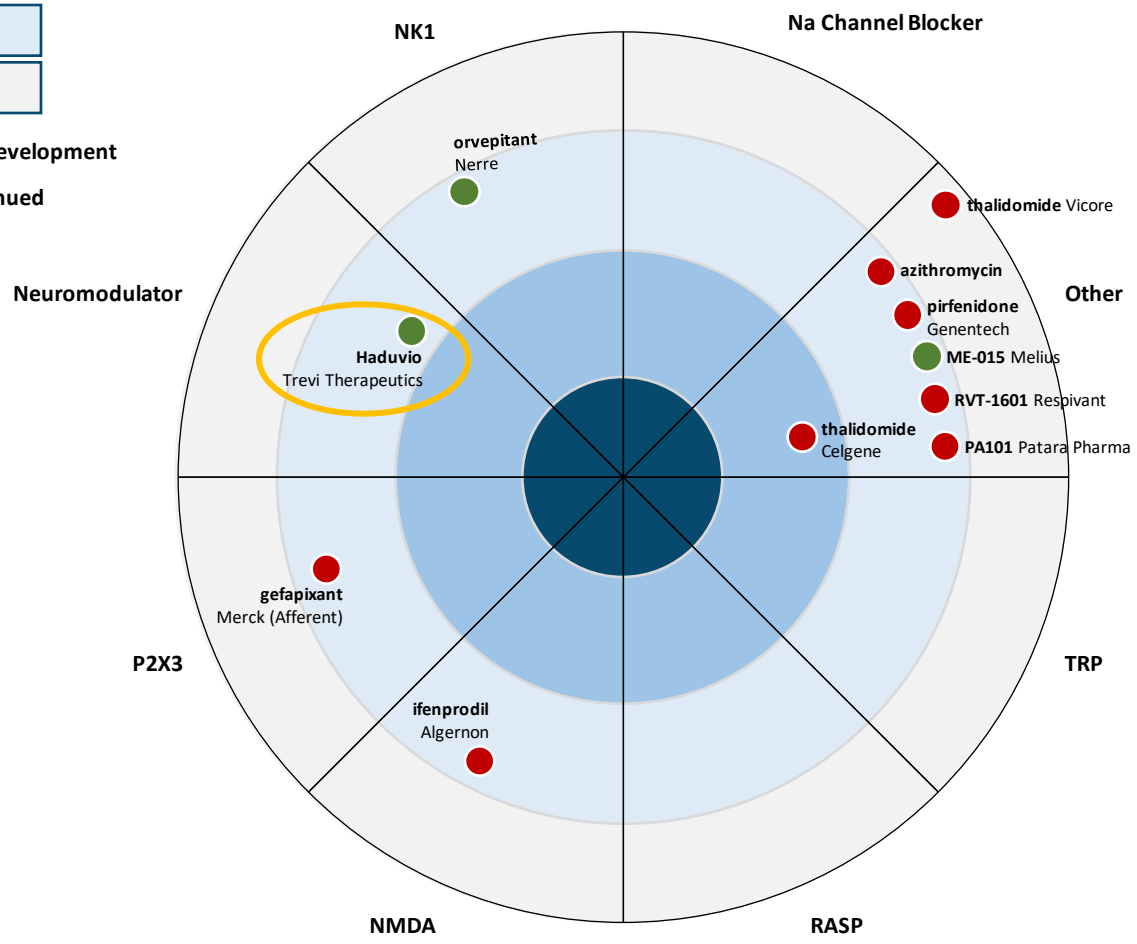
[1]2027 est. The Insight Partners Jun 2020

Opportunity for Haduvio to be Best-In-Class Across Chronic Cough Indications and First-In-Class in IPF

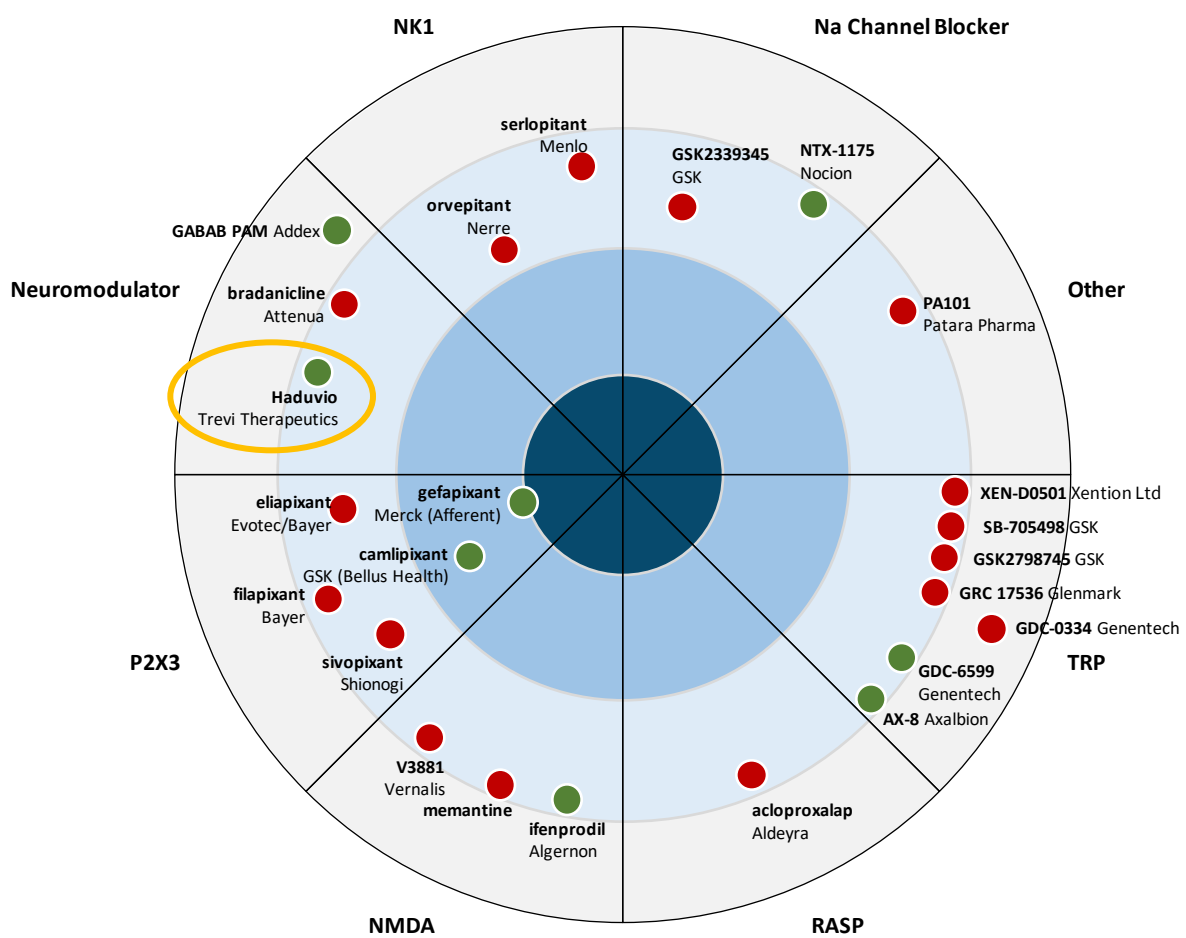
Registration
Phase 3
Phase 2
Phase 1

Active Development
Discontinued

IPF Chronic Cough



Refractory Chronic Cough



[1]Haduvio, Trevi Therapeutics: http://dx.doi.org/10.1136/thorax-2022-BTSabstracts.21 [2]Orvepitant, Nerre: https://classic.clinicaltrials.gov/ct2/show/NCT05185089?term=NCT05185089&draw=2&rank=1 [3]Morphine Sulfate, NHS: : 10.1186/s13063-022-06068-4. [4]Gefapixant, Merck: doi: 10.1007/s41030-021-00162-9 [5]Ifenprodil, Algernon: Algernon Pharmaceuticals Press Release January 9, 2023 [6]Thalidomide, Celgene: doi: 10.7326/0003-4819-157-6-201209180-00003. [7]Azithromycin: doi: 10.1513/AnnalsATS.202103-266OC. [8]ME-015, Melius: https://classic.clinicaltrials.gov/ct2/show/NCT05983471?term=melius&cond=Idiopathic+Pulmonary+Fibrosis&draw=2&rank=1 [9]Thalidomide, Vicore: https://vicorepharma.com/our-programs/rare-lung-diseases/talidomide-ipf-cough/ [10]Pirfenidone, Genentech: doi:10.1183/13993003.01157-2017. [11]RVT-1601, Respivant: doi: 10.1164/rccm.202106-1485OC [12]PA101, Patara: doi: 10.1016/S2213-2600(17)30310-7. [13]Haduvio, Trevi Therapeutics: Trevi Therapeutics Press Release January 5, 2023 [14]GABAB PAM, Addex: Addex Therapeutics Corporate Presentation August 2023 [15]Orvepitant, Nerre: Nerre Therapeutics Press Release June 7, 2019 [16]Serlopitant, Menlo: Menlo Press Release Oct 08, 2018 [17]Eliapixant, Evotec: doi.org/10.1164/ajrccm-conference.2022.205.1_MeetingAbstracts.A4776 [18]Gefapixant, Merck: doi: 10.1016/S0140-6736(21)02348-5 [19]Filapixant, Bayer: doi: 10.1186/s12931-023-02384-8. [20]Camlipixant, GSK: Bellus Health Press Release December 13, 2021 [21]Sivopixant, Shionogi: doi: 10.1007/s00408-022-00592-5 [22]V3881, Vernalis: Young E. et al. Lung. 2012;19:63. [23]Ifenprodil, Algernon: Algernon Pharmaceuticals Press Release January 9, 2023 [24]Memantine: doi:10.1183/23120541.00447-2021. [25]ADX-629 (acloproxalap), Aldeyra: Aldeyra Press Release Jan 4, 2024 [26]GRC 17536, Glenmark: doi: 10.1002/cpt.2003. [27]GDC-6599, Genentech: https://classic.clinicaltrials.gov/ct2/show/NCT05660850?term=GDC-6599&cond=chronic+cough&draw=2&rank=1 [28]GSK2798745, GSK: doi:10.1183/23120541.00269-2021. [29]SB-705498, GSK: doi:10.1016/j.jaci.2014.01.038. [30]AX-8, Axalbion: Axalbion Press Release May 22, 2023. [31]XEN-D0501, Xention LTD: Belvisi MG. et al. Am J Respir Crit Care Med. 2017 Nov 15;196(10):1255-1263 [32]Bradanicline, Attenua, Inc: doi:10.1183/13993003.congress-2020.4564 [33]NTX-1175, Nocion: Nocion Therapeutics Press Release August 31, 2021 [34]GSK2339345, GSK: doi: 10.5414/CP202804.

IPF
Chronic Cough

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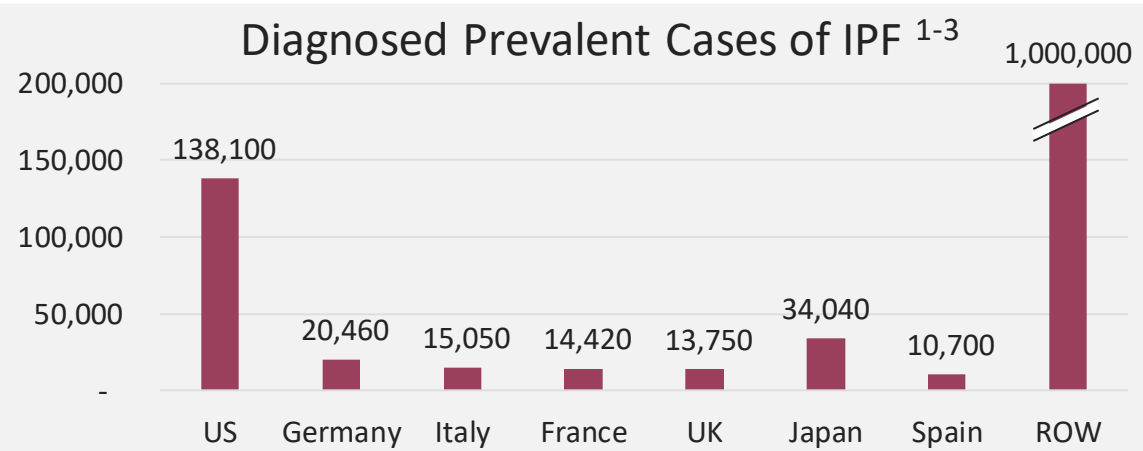
The Significant Role of Chronic Cough in IPF

Epidemiology



30,000-40,000

Incident cases of IPF in the US every year [4]

Up to 1,500 coughs

per day in an IPF patient.[5,6] The urge to cough cannot be relieved by coughing. [7]

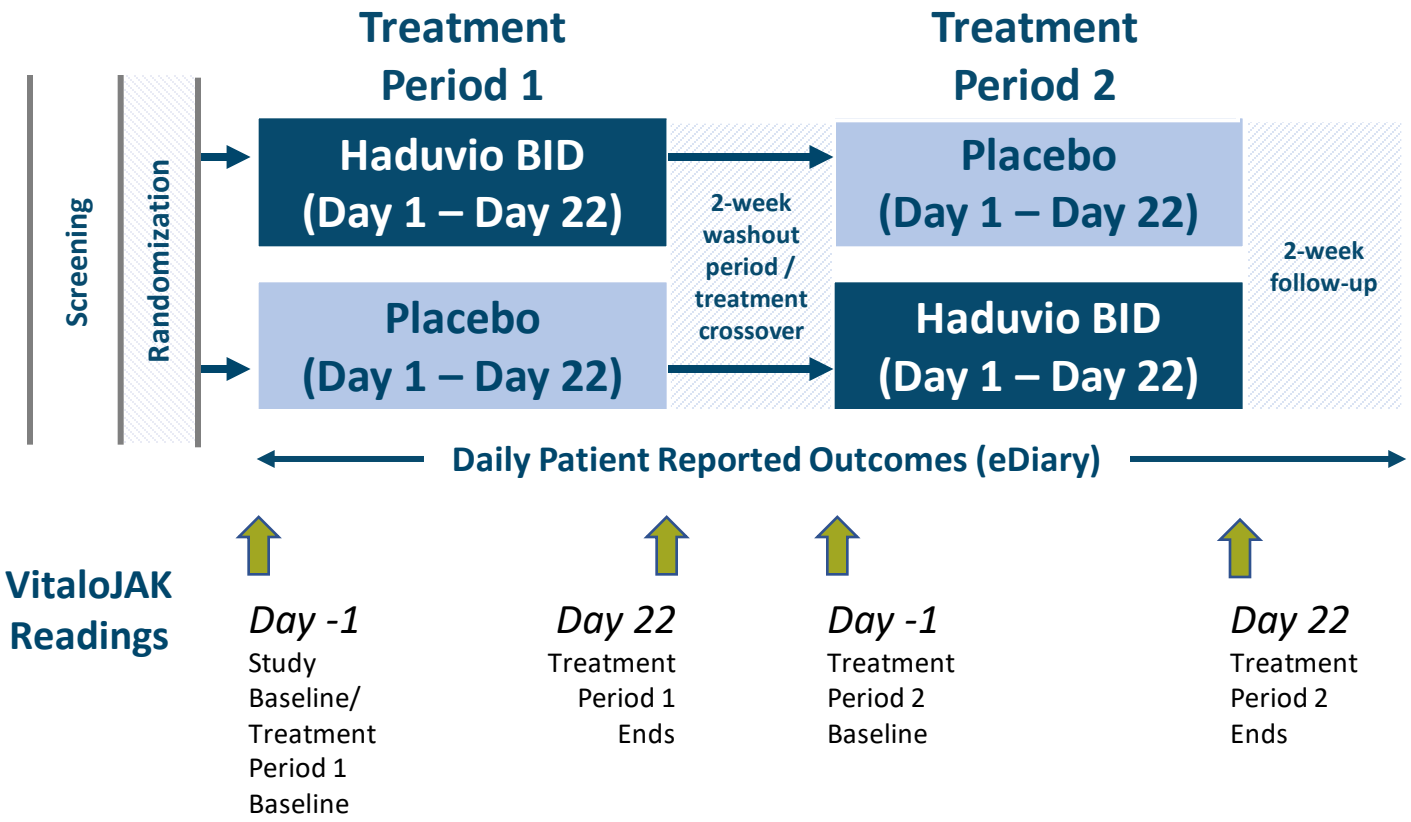
~85% of IPF Patients

experience chronic cough [8]

- **IPF is a high burden disease** that has a significant impact on QoL, e.g.: [5-10]
  - Coughing can increase feelings of anxiety as it induces breathlessness
  - Coughing spells or episodes lead to significant fatigue, air hunger, peripheral oxygen desaturation
  - The social impact and isolation of chronic cough in IPF further compounds limited exercise ability, reduced walking distance and the need to use supplemental oxygen
- Chronic cough may also **contribute to enhanced activation of profibrotic** mechanisms and **disease worsening in IPF** [11]
- Cough may be an **early clinical marker of disease activity**, may identify patients at high risk of progression, and may predict time to lung transplantation or death [8,12]

[1]Datamonitor 2015 Idiopathic Pulmonary Fibrosis Disease Coverage Ref Code: DMKC12770 [2]Kondoh Y et al. Respiratory Research 2022 DOI:10.1186/s12931-022-01938-6 [3]Natsuizaka M et al. Am J Respir Crit Care Med DOI: 10.1164/rccm.201403-0566OC [4]Nalysnyk L et al. Eur Resp Rev 2012 DOI: 10.1183/09059180.00002512 [5]Key AL et al. Cough 2010 DOI:10.1186/1745-9974-6-4 [6]VanManen M et al. Am J Respir Crit Care Med 2015; 191: A4422 [7]Swigris JJ et al. Health Qual Life Outcomes 2005 DOI: 10.1186/1477-7525-3-61 [8]Ryerson CJ et al. *Resp* 2011 DOI: 10.1111/j.1440-1843.2011.01996.x [9]vanManen M et al. *Ther Adv Respir Dis* 2017 DOI: 10.1177/1753465816686743 [10]Wakwaya Y et al. *Chest* 2021 DOI: 10.1016/j.chest.2021.05.071 [11]VanManen M et al. ERS 2016 DOI: 10.1183/16000617.0090-2015 [12]Lee J et al. Chest. 2022 Sep;162(3):603-613. DOI: 10.1016/j.chest.2022.03.025. Epub 2022 Mar 23.

IPF Chronic Cough CANAL Ph2a Trial Design
Randomized, Double-Blind, Placebo-Controlled, Two Treatment Period Crossover



Haduvio
Oral tablet dosed BID
Titrated to 162mg over the active treatment period

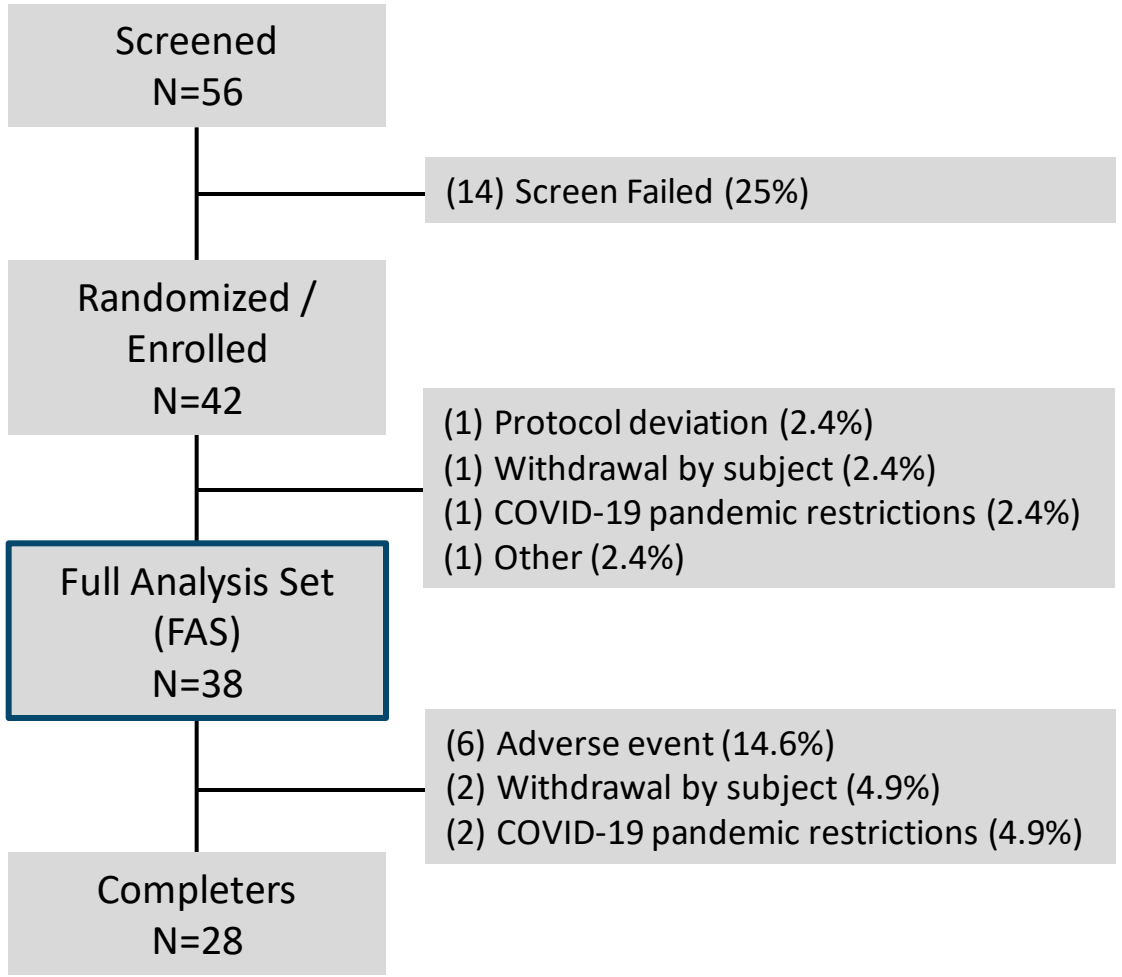
The VitaloJAK® Cough Monitor provides a fully validated system for objective measurement of cough.

Validated, 510k cleared and CE marked medical device system.

www.clinicaltrials.gov: NCT04030026
Haduvio (nalbuphine ER) is an investigational drug
BID: twice daily, VitaloJAK is a registered trademark of Vitalograph

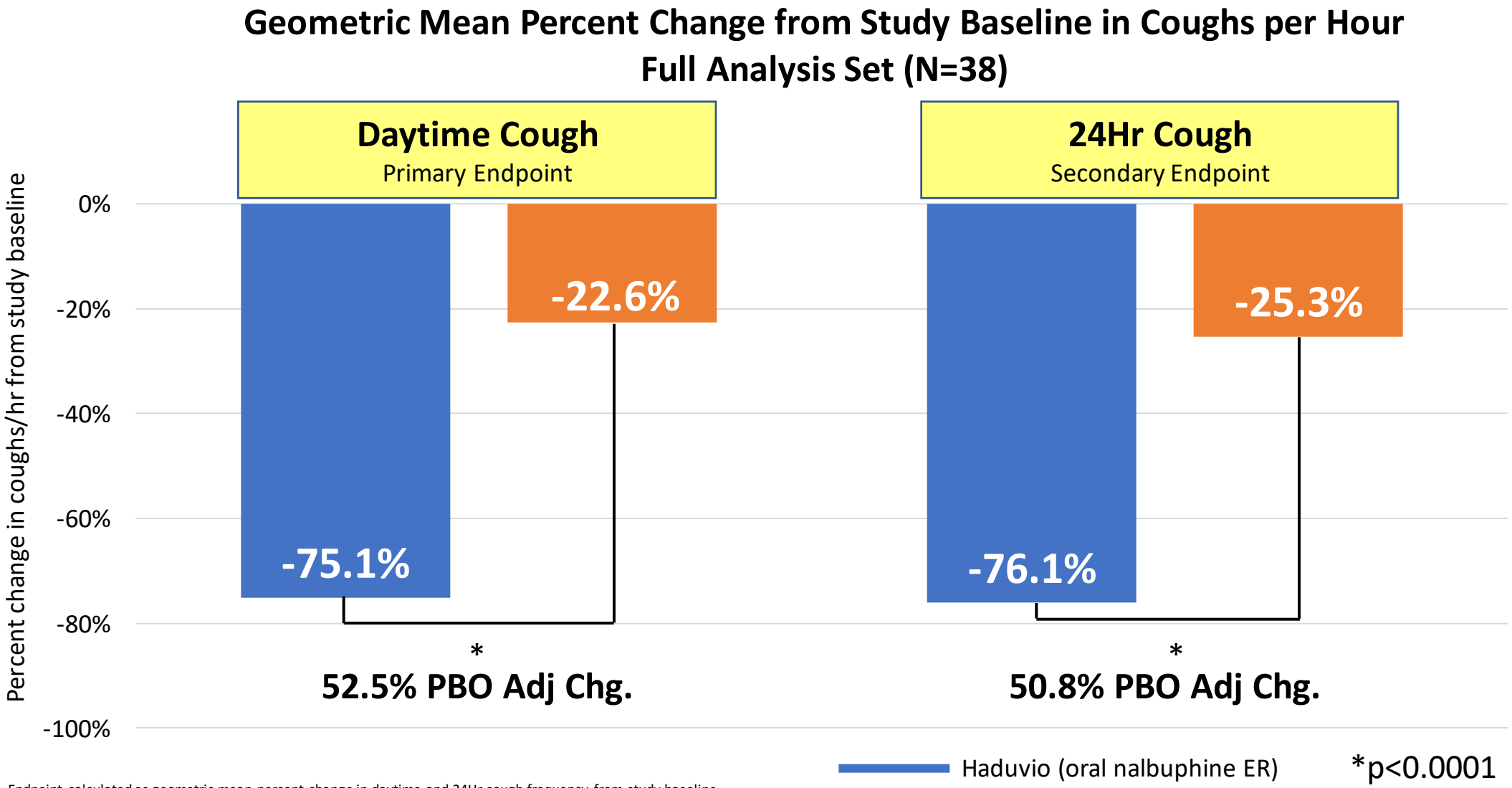
Baseline Characteristics and Patient Disposition

	Full Analysis Set (Subjects Completing ≥1 Treatment Period)
Number of subjects, n	38
Age (years), mean	74
Male, n (%)	32 (84.2%)
Anti-fibrotic (%)	21 (51.2%)
Daytime cough frequency (coughs/hr):	
Mean	28
Min-Max	3.18 - 92.35
24Hr cough frequency (coughs/hr):	
Mean	21
Min-Max	3.13 - 66.42



Full analysis set (FAS): all randomized subjects who have taken at least one dose of study medication and provided baseline and at least one post-baseline primary efficacy variable assessment during the treatment period.
Completers analysis set: all subjects who received both study treatments and completed both treatment periods in the study.
Haduvio (nalbuphine ER) is an investigational drug

Reduction of Cough Frequency And Placebo-Adjusted Change Were Consistent Between Daytime and 24Hr Cough Frequency



Endpoint calculated as geometric mean percent change in daytime and 24Hr cough frequency from study baseline
No sequence or period effect
Haduvio (nalbuphine ER) is an investigational drug

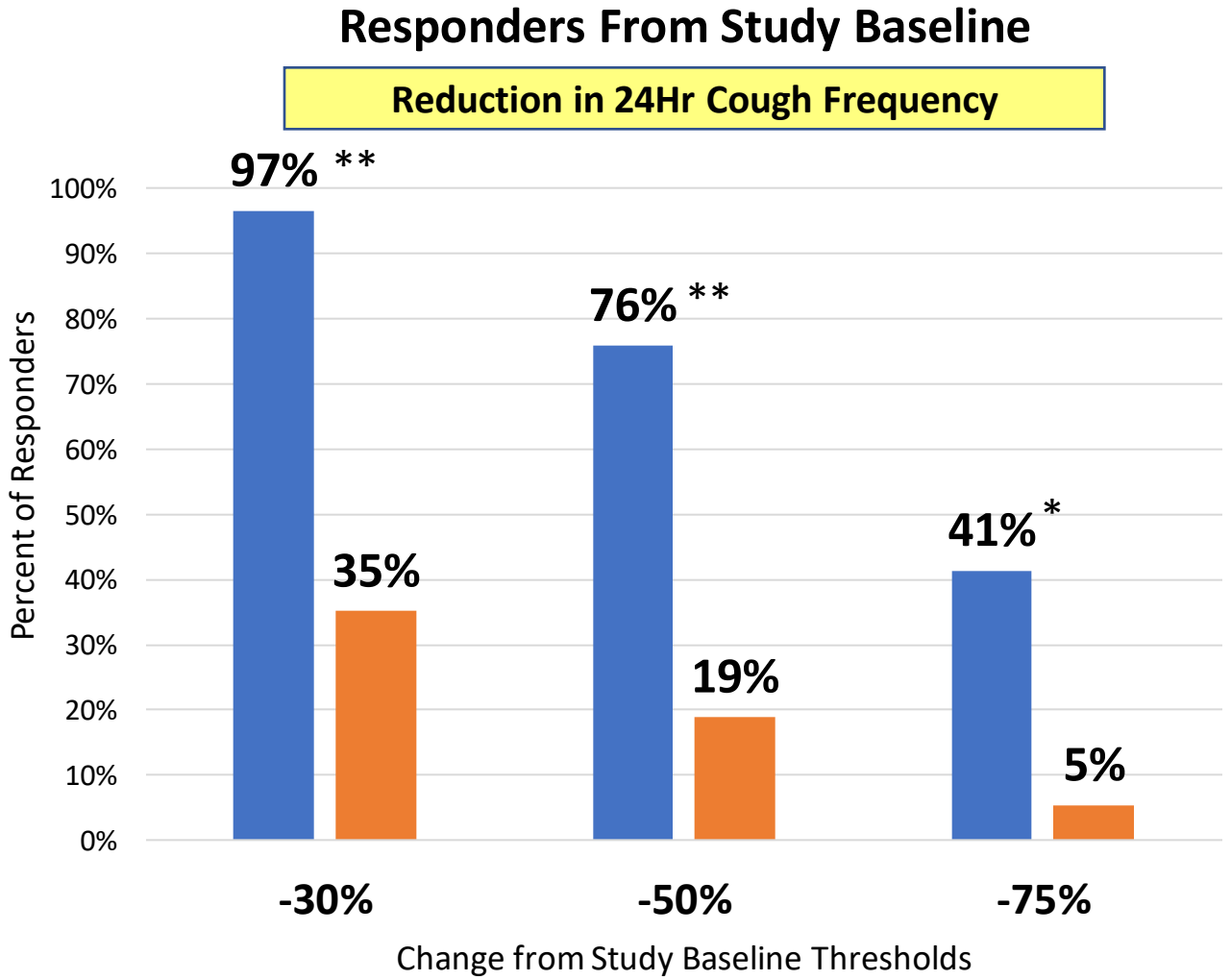
Post-Hoc Responder Analyses
Clear Separation Between Haduvio vs. Placebo at All Thresholds

97% of Haduvio subjects

saw a clinically meaningful reduction in 24Hr cough frequency

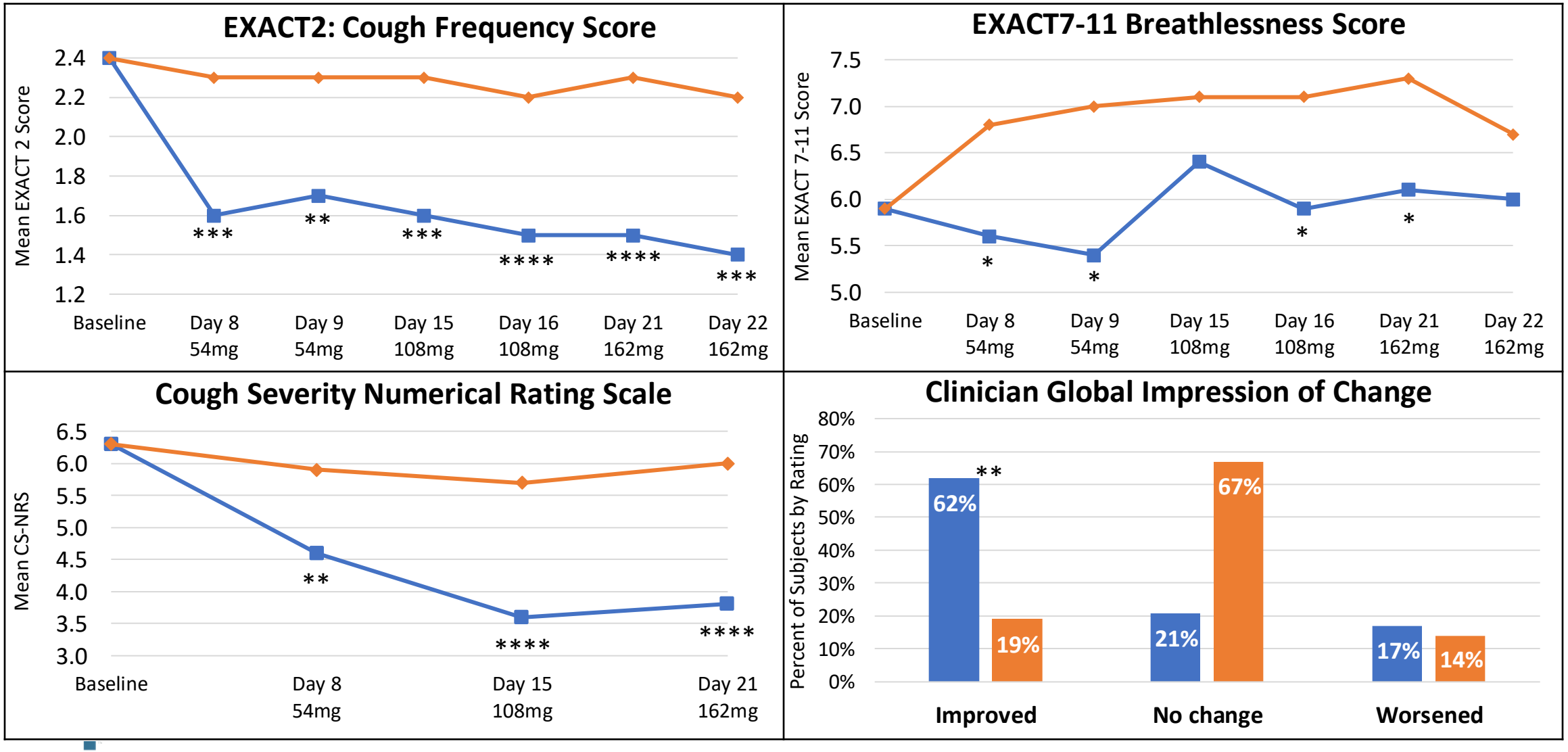
(Subjects experiencing a 20-30% reduction in their cough frequency is considered clinically meaningful)[1]

76% of Haduvio subjects reduced their cough frequency in half



[1]Nguyen AM et al. J Allergy and Clin Immunol 2019 doi.org/10.1016/j.jaci.2018.12.519
Endpoint calculated as geometric mean percent change in 24Hr cough frequency from study baseline
Haduvio (nalbuphine ER) is an investigational drug

Patient and Clinician Reported Outcomes Support the Results Seen in the Objective Cough Monitor on the Full Analysis Set (N=38)



EXACT2, EXACT7-11, and CS-NRS endpoints calculated as mean outputs change from baseline. CGI-C calculated as percent of subjects seeing improvement/decline vs. study baseline
Haduvio (nalbuphine ER) is an investigational drug

Haduvio (oral nalbuphine ER)
Placebo

*p≤0.05 **p≤0.01 ***p≤0.001 ****p≤0.0001

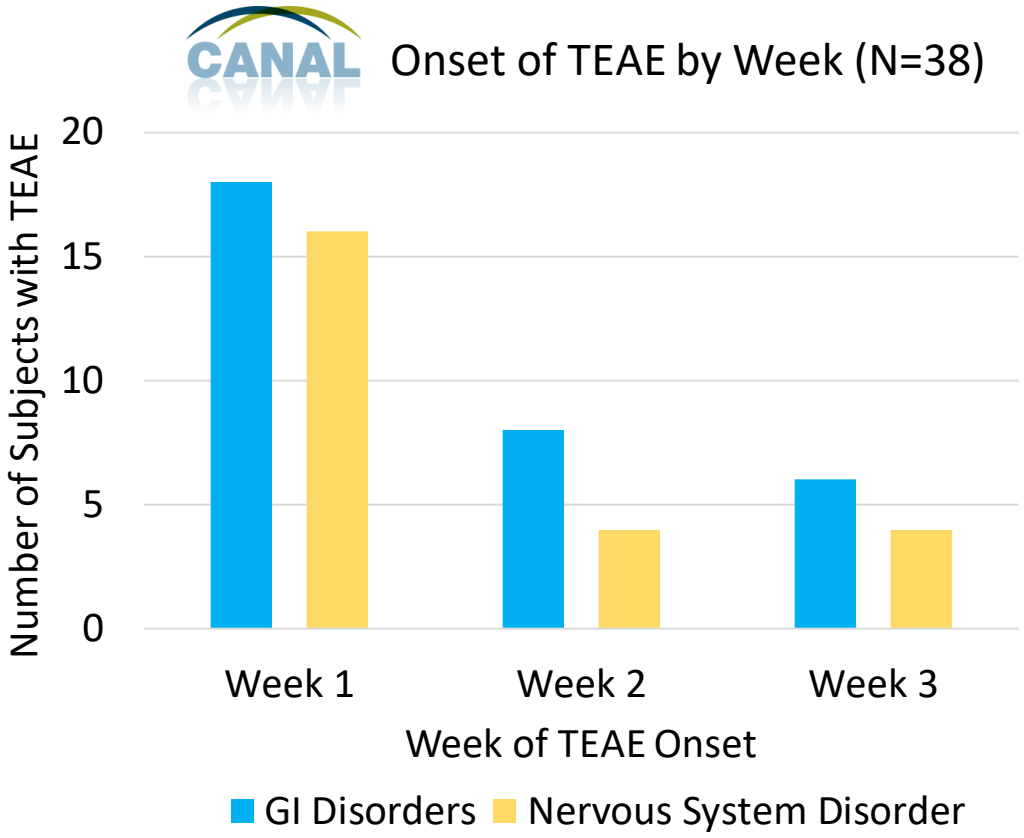
Summary of Treatment-Emergent Adverse Events by CTCAE Grade Safety Population[1]

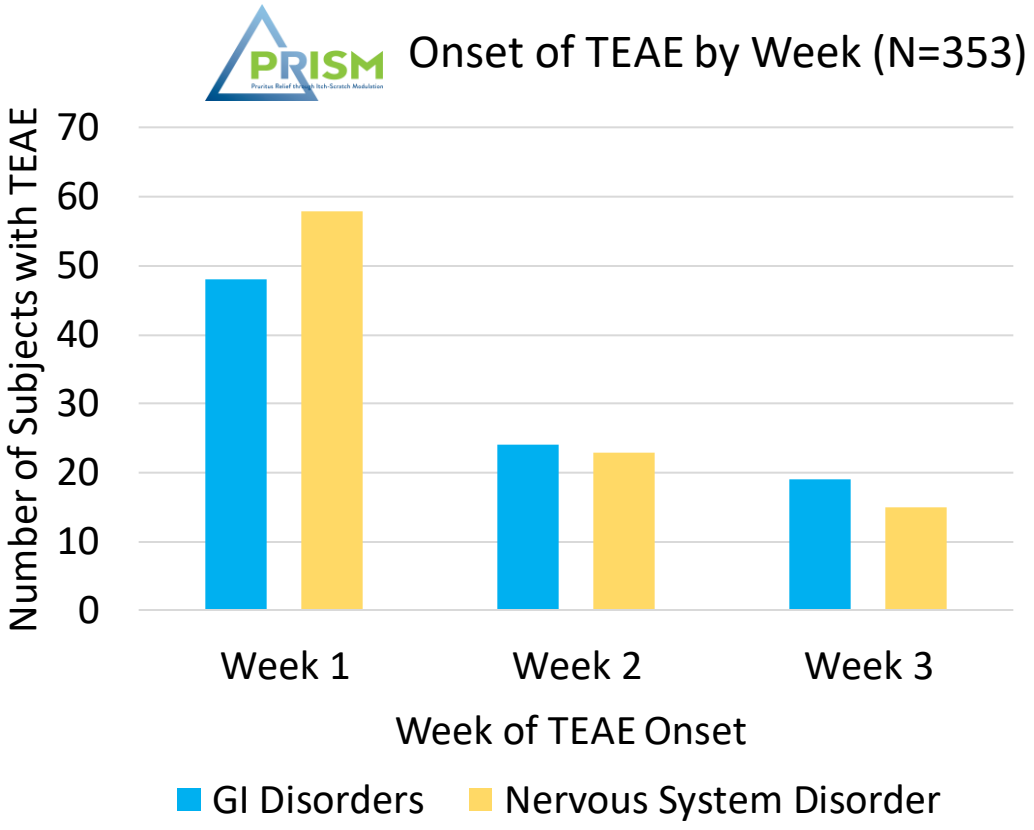
	Haduvio N=38 n (%)			Placebo N=40 n (%)			Total N=41 n (%)		
GRADE	1	2	3	1	2	3	1	2	3
Nausea	9 (24)	7 (18)	-	-	-	-	9 (22)	7 (17)	-
Fatigue	8 (21)	3 (8)	1 (3)	1 (3)	1 (3)	1 (3)	9 (22)	4 (10)	2 (5)
Constipation	8 (21)	3 (8)	-	1 (3)	1 (3)	-	9 (22)	4 (10)	-
Dizziness	7 (18)	3 (8)	-	-	-	-	7 (17)	3 (7)	-
Somnolence	7 (18)	2 (5)	-	1 (3)	-	-	7 (17)	2 (5)	-
Vomiting	4 (11)	3 (8)	-	5 (13)	-	-	7 (17)	3 (7)	-
Headache	2 (5)	3 (8)	-	5 (13)	-	-	7 (17)	3 (7)	-
Anxiety	2 (5)	1 (3)	2 (5)	-	-	-	2 (5)	1 (2)	2 (5)
Depression	3 (8)	-	1 (3)	-	-	-	3 (8)	-	1 (2)

[1] One subject may have multiple Adverse Events
Summary of Treatment-Emergent Adverse Events by CTCAE Grade - Safety Population
Haduvio (nalbuphine ER) is an investigational drug

Adverse Events Occur Early in Treatment and Generally Last 3-6 Days

CANAL Consistent with Previous Studies Including PRISM

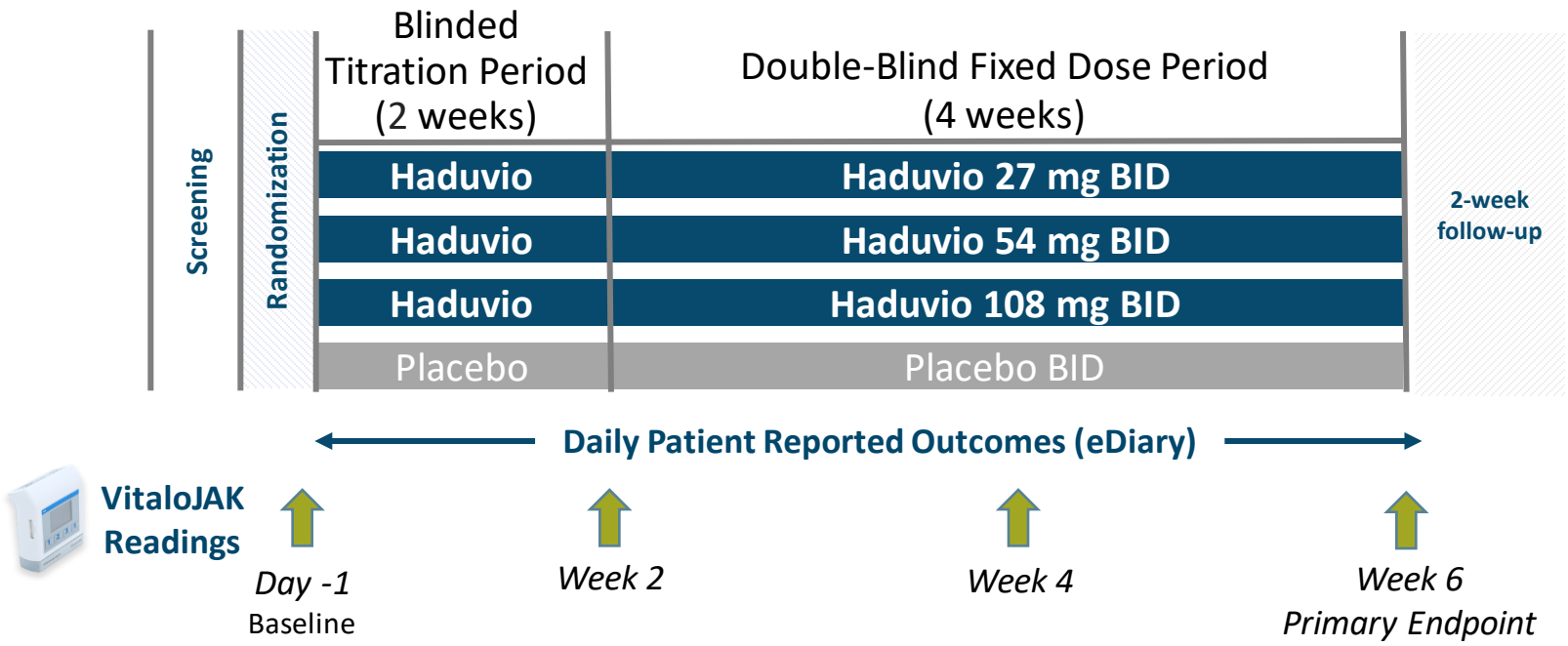




Duration of Adverse Events: 3-6 Days

TEAE = Treatment Emergent Adverse Event, Onset of TEAE and duration of TEAE based on median number of days
One subject may have multiple Adverse Events. Data is based on the safety population for the primary endpoint at 14 weeks.
Haduvio (nalbuphine ER) is an investigational drug

IPF Chronic Cough Dose-Ranging Ph2b Trial Design (N ~160)



Design

Randomized, double-blind, placebo-controlled, parallel-arm design

Primary Efficacy Endpoint:

- 24-hour cough frequency via VitaloJAK

Sample Size Re-estimation (SSRE) performed after 50% of subjects complete

Secondary Endpoints:

- EXACT2 – Cough frequency score (Key secondary)
- EXACT:IPF, CS-NRS, LCQ, L-IPF, EQ-5D-5L
- PGI-S & PGI-C Cough, PGI-S & PGI-C IPF
- SOWS
- CGI-C, CGI-S

Initiated in 4Q 2023, SSRE expected 2H 2024, and topline data expected 1H 2025*

Design plan subject to discussions with regulatory authorities

Haduvio (nalbuphine ER) is an investigational drug, *Expected topline data from CORAL dependent on SSRE results

BID: twice daily, 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, SOWS: Subject Opiate Withdrawal Scale, CGI-S: clinician global impression of cough severity, CGI-C: clinician global impression of change of cough

Refractory Chronic Cough

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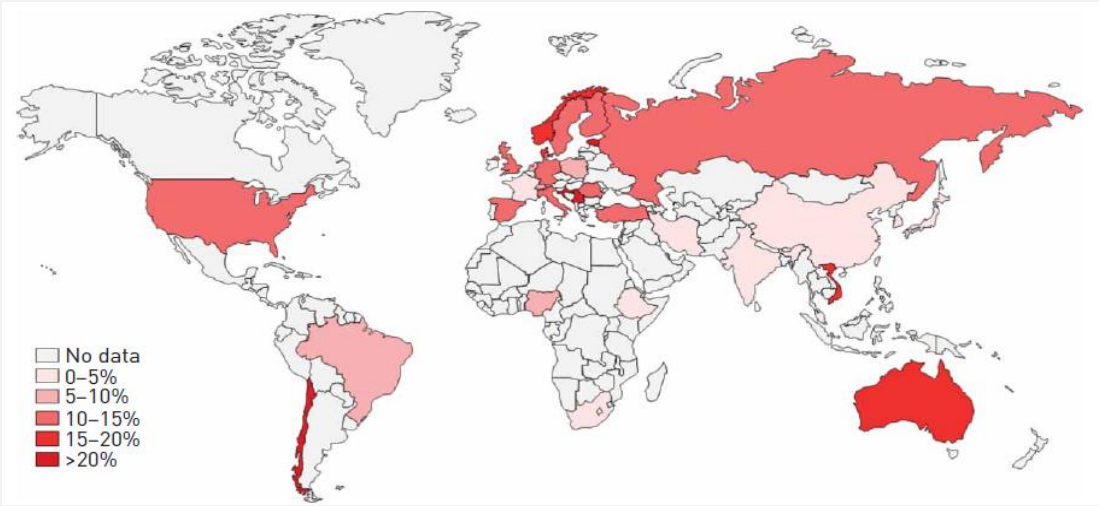
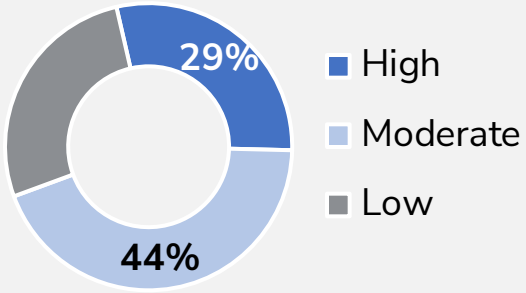
The Significant Impact of Refractory Chronic Cough (RCC)

~5-10% Global Prevalence of Chronic Cough[1]

RCC Treatable U.S. Patient Population: ~2-3M Patients



Cough Frequency in RCC[2]



~72% of RCC patients are uncontrolled

(among high and moderate frequency coughers)[2]

- For adult patients, chronic cough is a cough that lasts for >8 weeks[3]
- **Refractory chronic cough is defined as a cough that persists despite guideline-based treatment[4]**
- RCC Phenotypes [4]
  - **Asthmatic** cough/ eosinophilic bronchitis
  - **GERD** cough (Gastroesophageal reflux disease)
  - **Postnasal drip** / upper airways cough syndrome
- **87%** of RCC patients have severe to moderate impact on Quality of Life [2]
- RCC patients experience physical, psychological, and social impacts on their quality of life[5-8]:
  - Chest pain, hernia, and urinary incontinence
  - Depression, sleep disturbances, dizziness, headaches, and physical exhaustion
  - Interruption of social interactions and embarrassment

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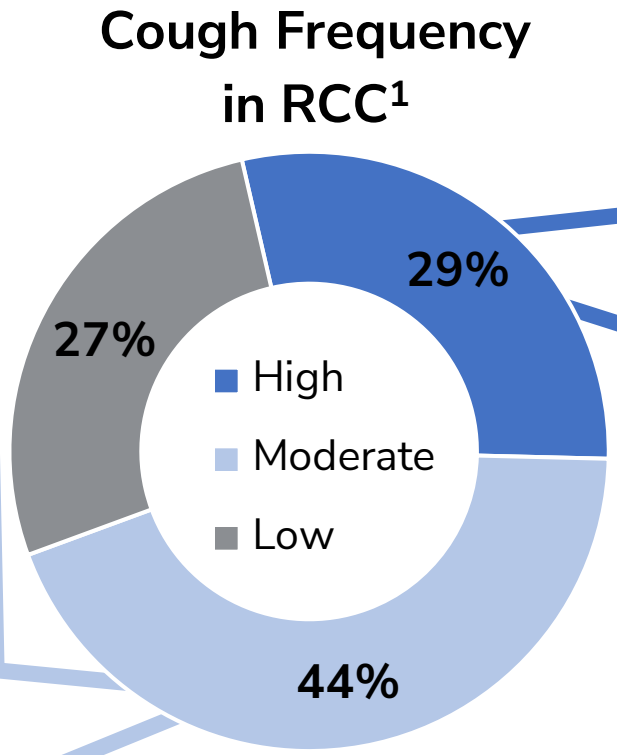
[1]Woo-Jung Song et al, ERJ 2015 doi: 10.1183/09031936.00218714 [2]LifeSci Capital Report Nov 2022, US (N=1000) [3]American College of Chest Physicians (ACCP) [4]Morice AH, et al. Eur Respir J. 2020 doi: 10.1183/13993003.01136-2019 [5]Dicpinigaitis PV et al. Chest 2006 doi 10.1378/chest.130.6.1839 [6]Chen, J et al. DMR 2022 doi: 10.21037/dmr-22-60[7]Kuzniar TJ et al. Mayo Clin Proc 2007 https://doi.org/10.4065/82.1.56 [8]French CL et al. Arch Intern Med 1998 doi: 10.1001/archinte.158.15.1657

Haduvio Is Well-Positioned for Potential Differentiation Across The Broadest Range of RCC Patients

RIVER 1:1 stratification in moderate coughers (n=30) and in severe coughers (n=30)



gefapixant[2] MERCK
Not significant in Ph3 trials

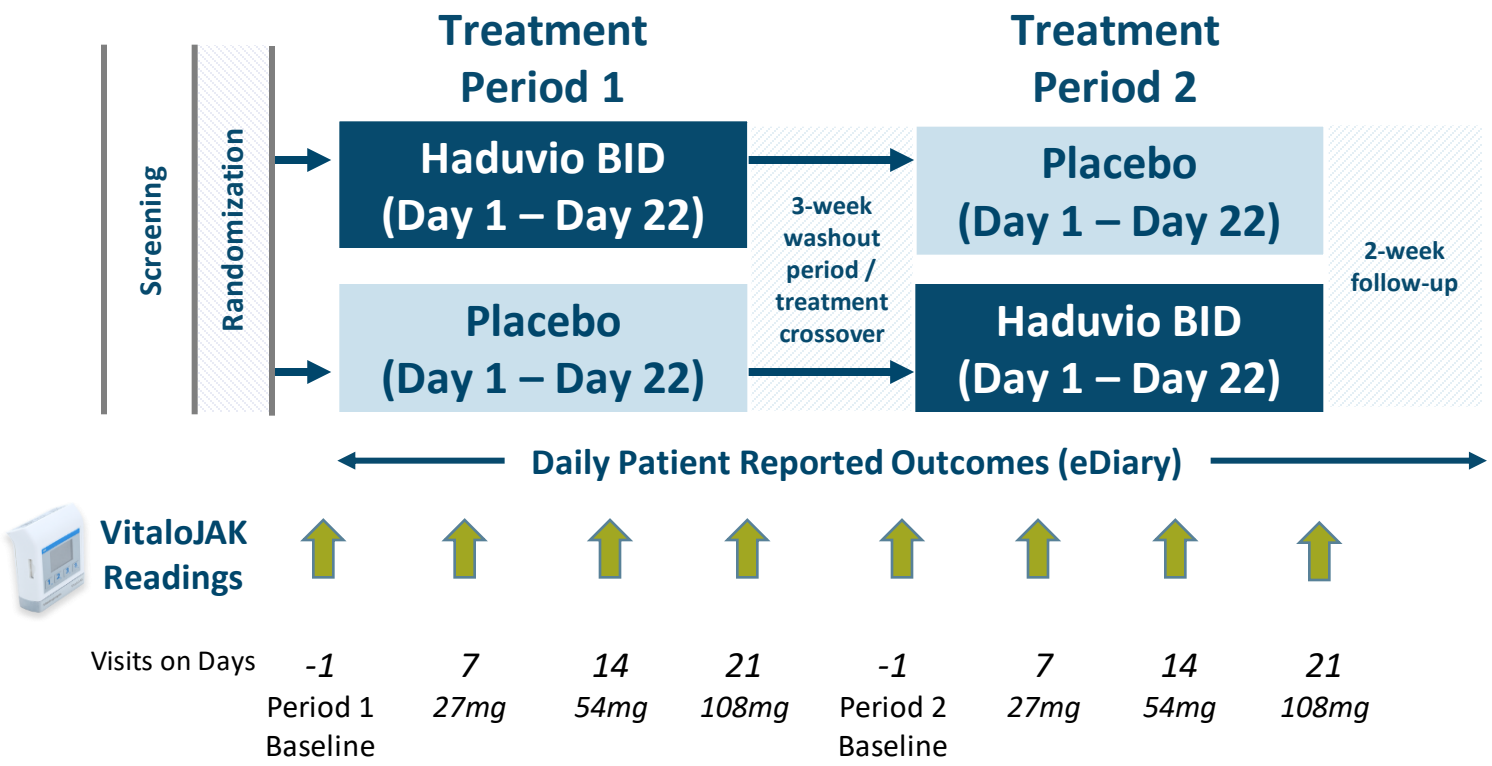
Camlipixant[3,4] GSK
Not significant in Ph2a trial
Not significant in Ph2b trial

gefapixant[5] MERCK
Ph3 subgroup statistically significant

Camlipixant[3,6] GSK
Ph2a pre-specified subgroup statistically significant
Ph2b statistically significant with 50mg and 200mg doses

[1]LifeSci Capital Report Nov 2022, US (N=1000) [2]McGarvey LP et al. Lancet. 2022 Mar 5;399(10328):909-923. doi: 10.1016/S0140-6736(21)02348-5 [3]Bellus Health Press Release January 21, 2021 [4]Bellus Health Data Presentation December 13, 2021
[5]Smith JA et al. Lung. 2022 Aug;200(4):423-429. doi: 10.1007/s00408-022-00553-y [6]Bonucelli C. et al International Cough Symposium January 23, 2021
Haduvio (nalbuphine ER) is an investigational drug.

Refractory Chronic Cough Ph2a Trial Design (N ~60)



Haduvio
Oral tablet dosed BID
Titrated to 108mg over the active treatment period

1:1 Stratification
10-19 coughs/hour (24hr)
≥20 coughs/hour (24hr)

Primary Efficacy Endpoint:
- 24-hour cough frequency via VitaloJAK

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

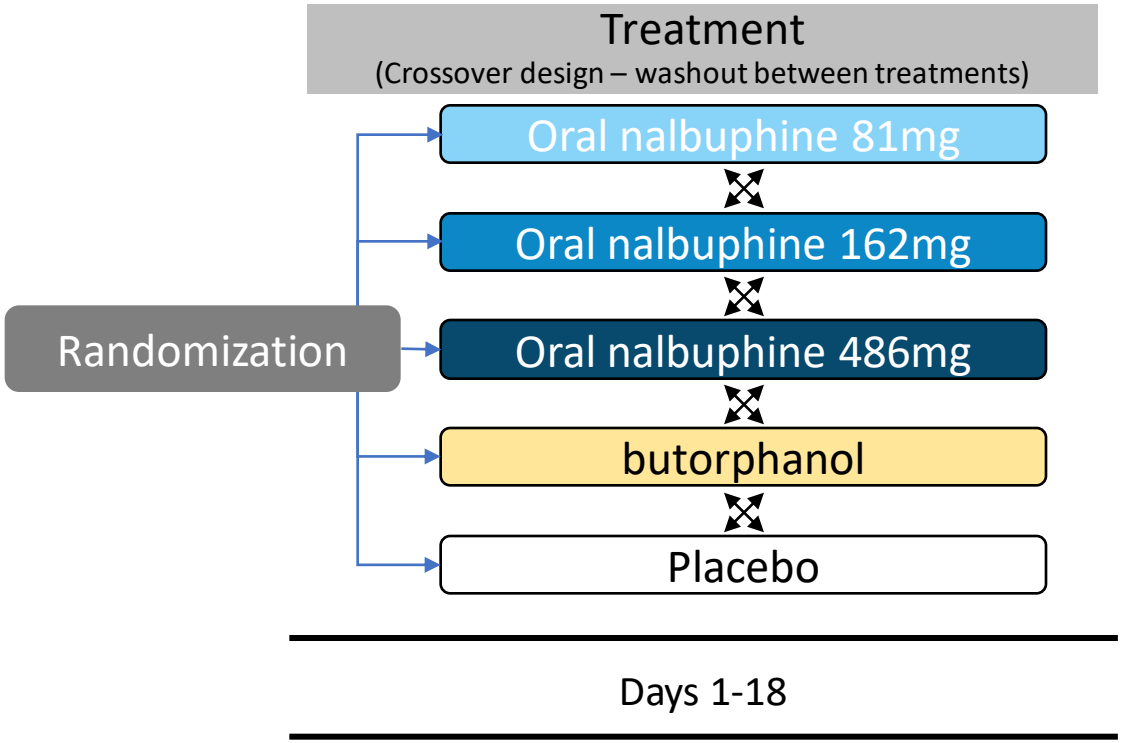
Initiated in 4Q 2023 and topline data expected 2H 2024

Haduvio (nalbuphine ER) is an investigational drug.
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

Human Abuse Potential (HAP) Comparative Study Design (N ~56)

Part 1
Characterized the active control comparator (butorphanol) PK/PD and selected butorphanol dose for Part 2

Part 2
A randomized, double-blind, double-dummy, active- and placebo-controlled 5-way crossover study



Objectives*

Primary Objective:
Evaluate abuse potential

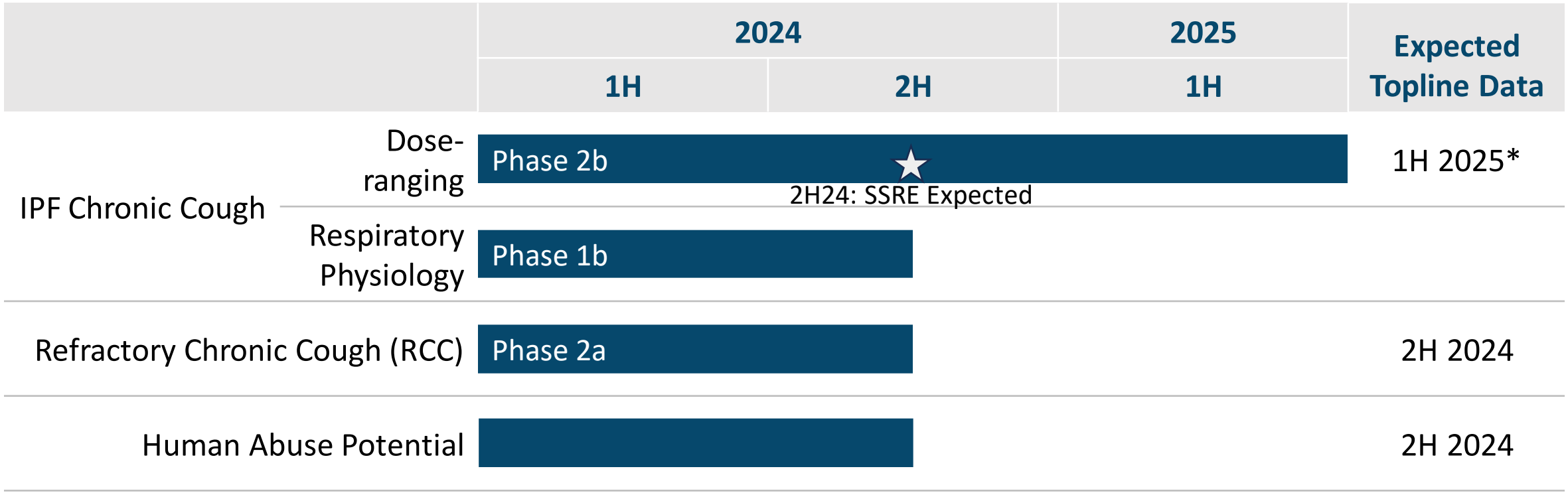
Primary Endpoint:
Peak (maximum) effect (Emax) for Drug Liking ("at this moment"), assessed on a bipolar, 100-point visual analog scale (VAS)

Secondary Objectives:
Assess PK, safety and tolerability

*Measuring oral nalbuphine relative to butorphanol and placebo.

Initiated in Q4 2023 and topline data expected 2H 2024

Multiple Clinical Data Read-outs Over Next 12-18 Months with Strong Cash Position



Cash and Investments

- $88.9M in cash and investments as of 9/30/2023
- Cash runway expected into 2026

Development plans subject to discussions with regulatory authorities
Haduvio (nalbuphine ER) is an investigational drug
*Expected topline data from CORAL dependent on SSRE results