Yale Innovation Summit

June 1, 2023

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 and plans with respect to future 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, future expenses and other financial results, including Trevi's ability to fund future operations, including clinical trials; uncertainties regarding the scope, timing and severity of the COVID-19 pandemic, the impact of the COVID-19 pandemic on Trevi's clinical operations and actions taken in response to the pandemic; as well as other risks and uncertainties set forth in the annual report on Form 10-Q for the quarter ended March 31, 2023 filed with the Securities and Exchange Commission and in subsequent filings with the Securities and Exchange Commission. All forward-looking statements contained in this press release 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.

Welcome

Jennifer Good
President and CEO

trevi™ THERAPEUTICS

Agenda

Jennifer Good
Trevi Therapeutics

Peter Dicpinigaitis, MD
Albert Einstein College of Medicine

Farrell Simon, Pharm.D.
Trevi Therapeutics

Welcome	**Jennifer Good**, President and CEO, Trevi Therapeutics, Inc.
Clinical Need for Chronic Cough Therapies and Mechanisms of Interest	**Peter Dicpinigaitis, MD**, Professor of Medicine at the Albert Einstein College of Medicine, in the Division of Critical Care Medicine
Unmet Patient Need in Chronic Cough and Commercial Potential of Haduvio	**Farrell Simon**, Chief Commercial Officer, Trevi Therapeutics, Inc.
Key Upcoming Milestones	**Jennifer Good**, President and CEO, Trevi Therapeutics, Inc.

Trevi Therapeutics: Two Successful Trials Validating the Mechanism in Hard to Treat Neuroinflammatory Conditions

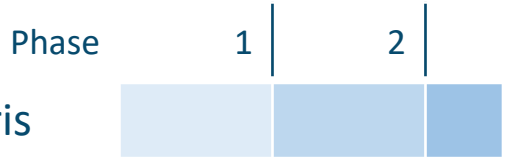
CANAL

Chronic Cough in Idiopathic Pulmonary Fibrosis (IPF)

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

PRISM
Pruritus Relief through Itch-Scratch Modulation

Prurigo Nodularis (PN)



- Trial achieved statistical significance on the primary and all key secondary endpoints
- Statistically significant for the primary efficacy endpoint measured by a 4-point reduction in the Worst Itch Numerical Rating Scale (WI-NRS) ($p=0.0157$)

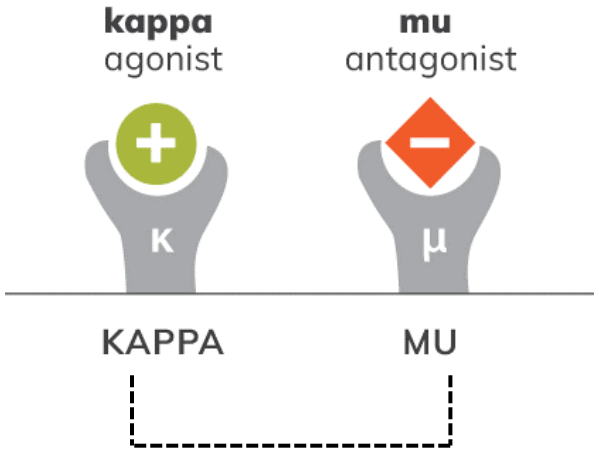
trevi THERAPEUTICS

Haduvio (nalbuphine ER) is an investigational drug

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

Novel Dual-Acting Mechanism of Action

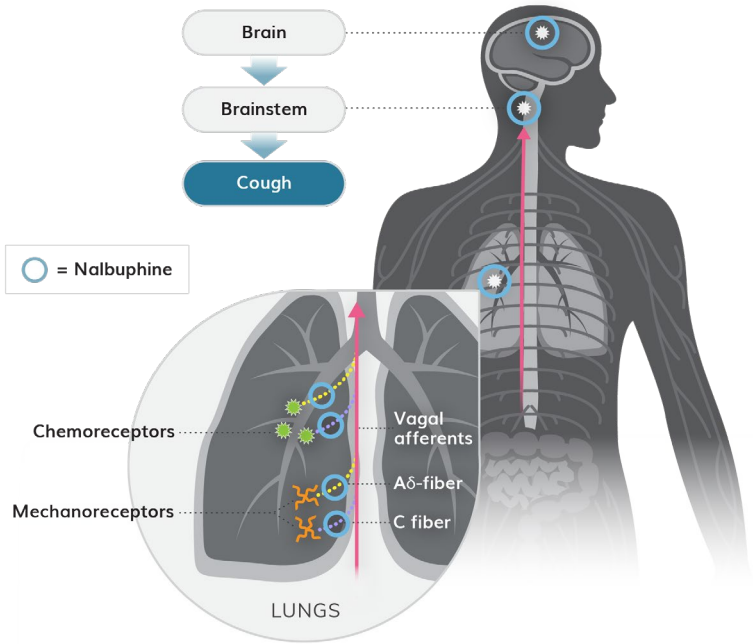
Kappa agonist and mu antagonist works across the neuroinflammatory axis to rebalance hypersensitivity conditions, such as chronic cough



Dynamic interchange between the two receptors

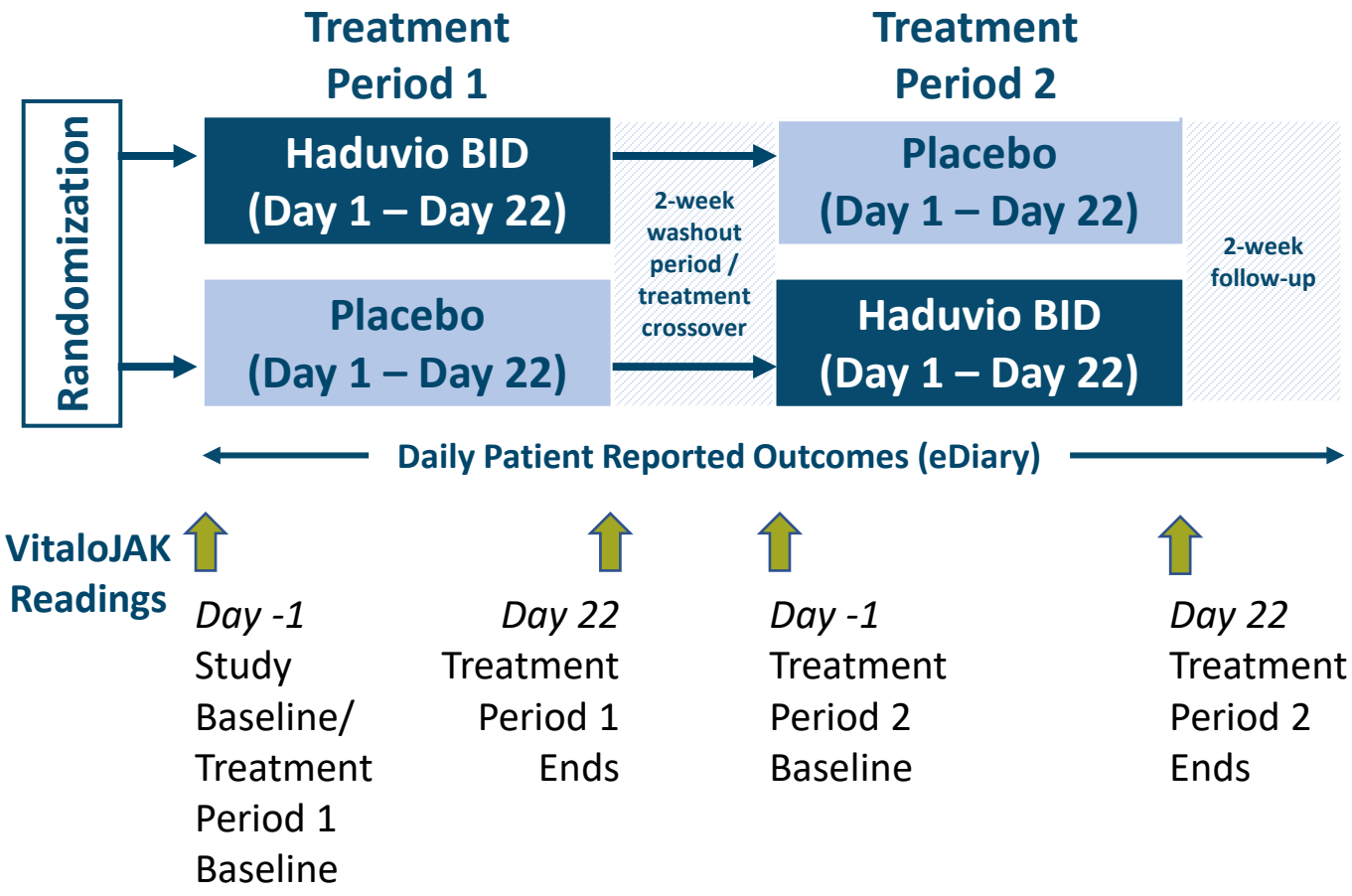
Importance of Central and Peripheral Activity

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

CANAL Phase 2 Trial Design
Randomized, Double-Blind, Placebo-Controlled, Two Treatment Period Crossover



HADUVIO

Oral tablet dosed BID

Titrated to 162mg over the active treatment period

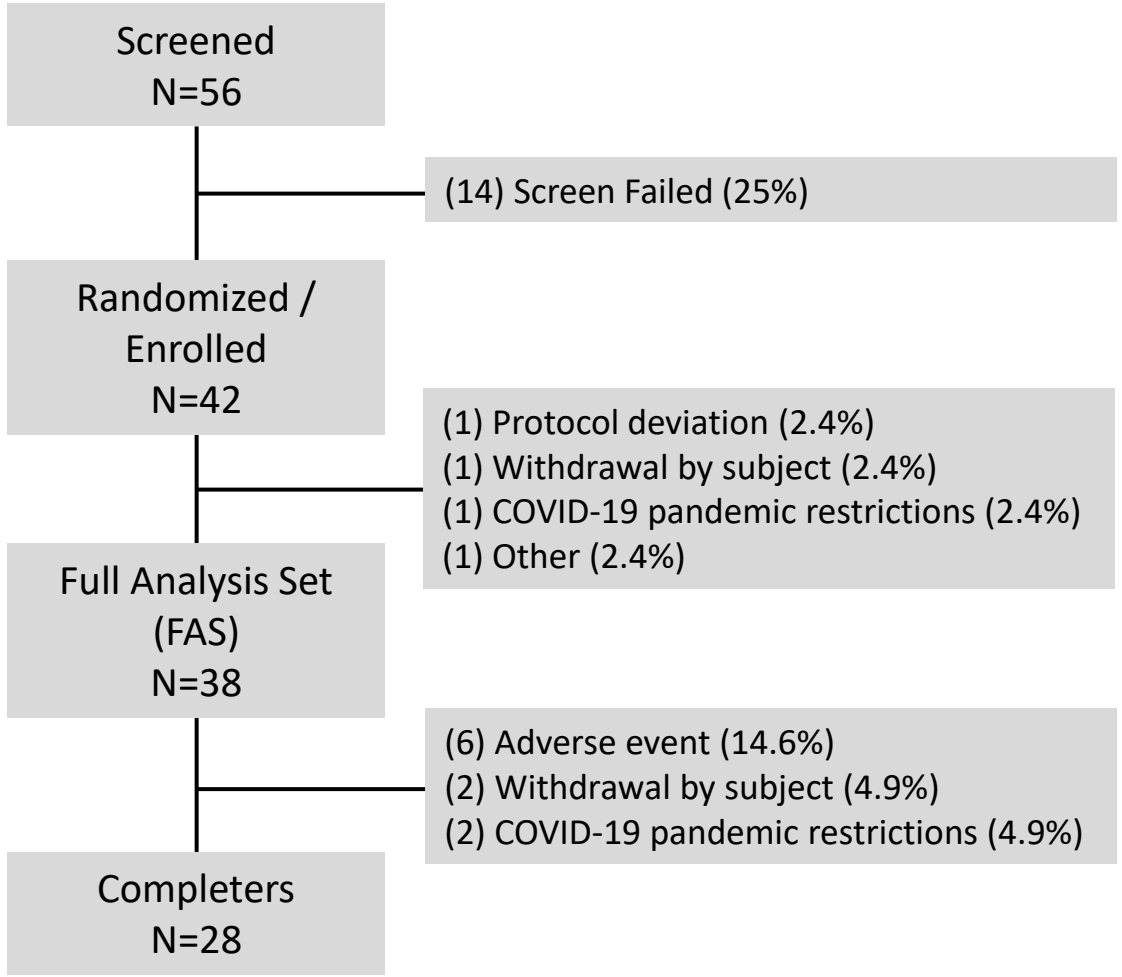
The VitaloJAK® Cough Monitor provides a fully validated system for objective measurement of cough.

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

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

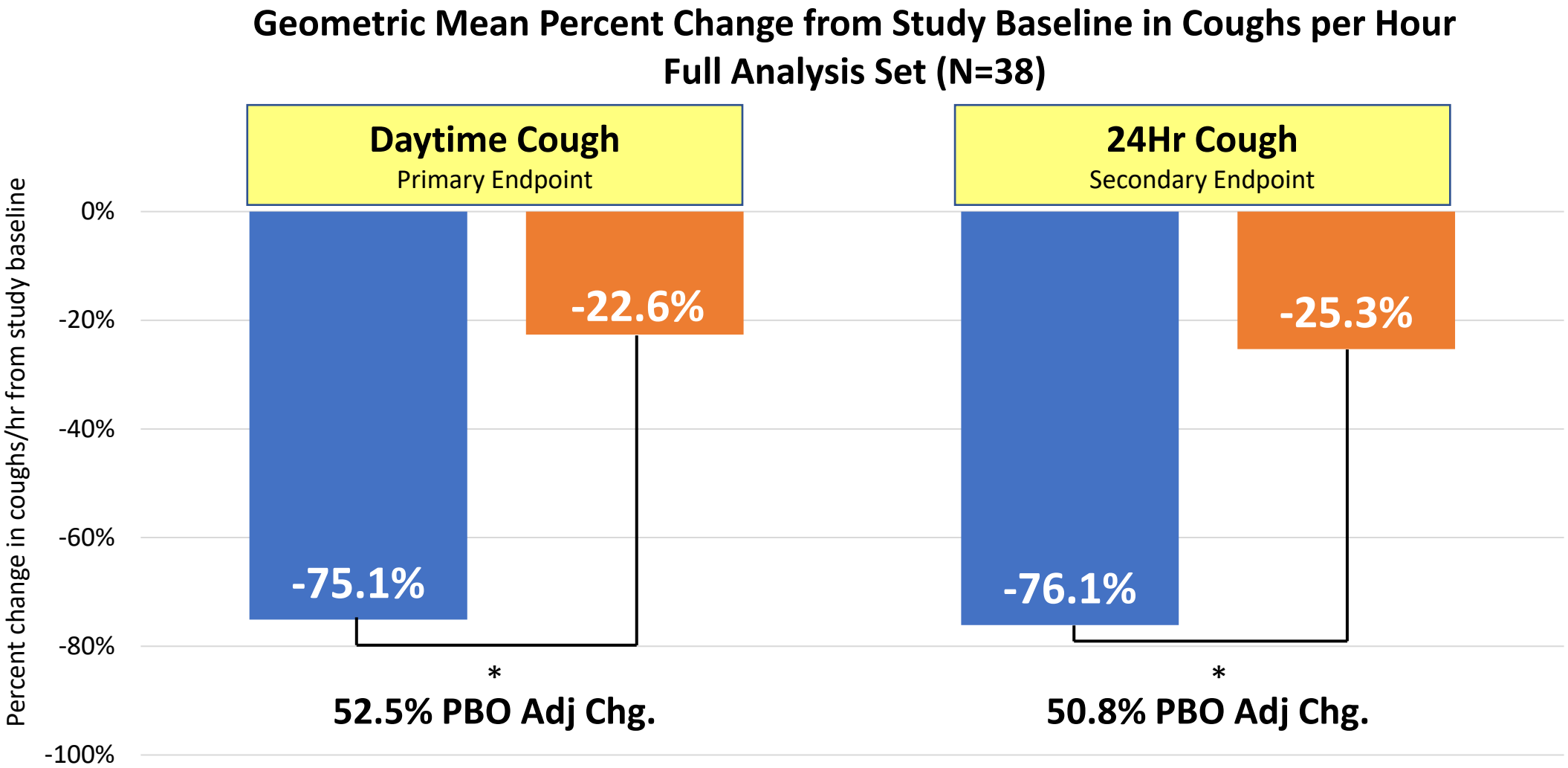
Baseline Characteristics and Patient Disposition

	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

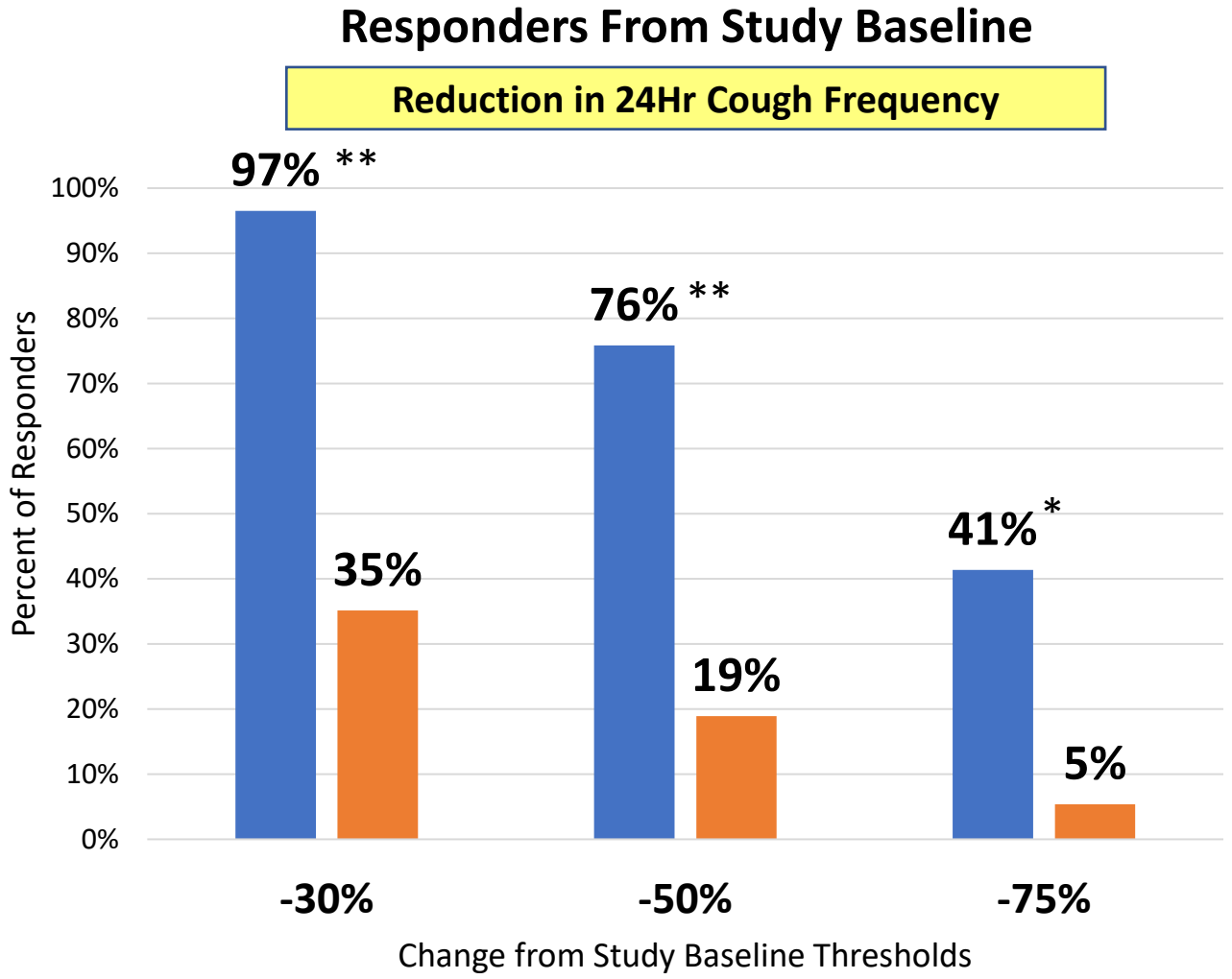
Post-Hoc Responder Analyses
Clear Separation Between Haduvio vs. Placebo at All Thresholds

97% of Haduvio subjects

saw a clinically meaningful reduction in 24Hr cough frequency

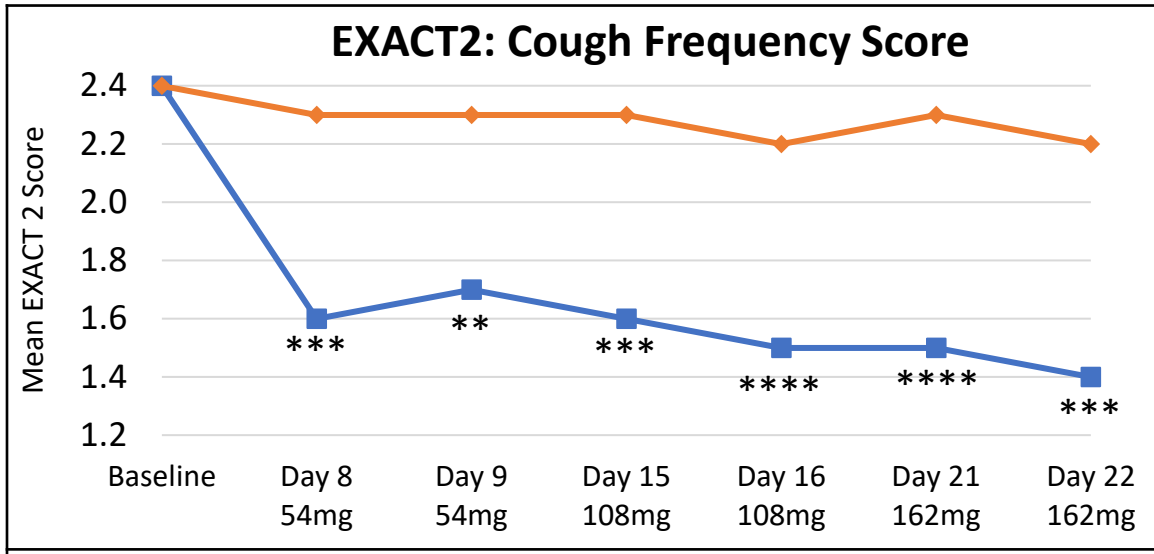
(Subjects experiencing a 20-30% reduction in their cough frequency is considered clinically meaningful)[1]

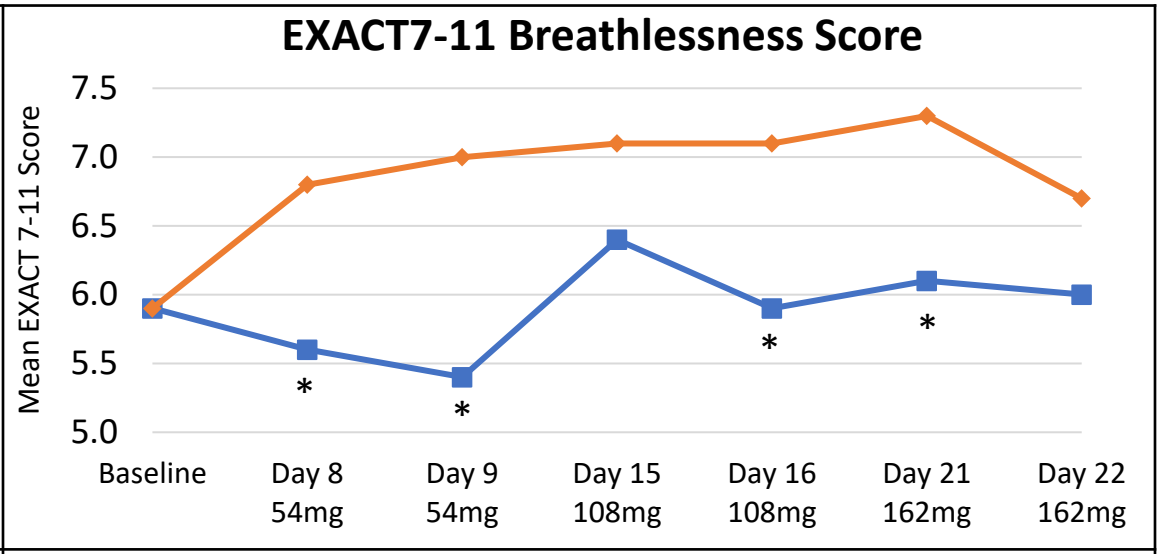
76% of Haduvio subjects reduced their cough frequency in half

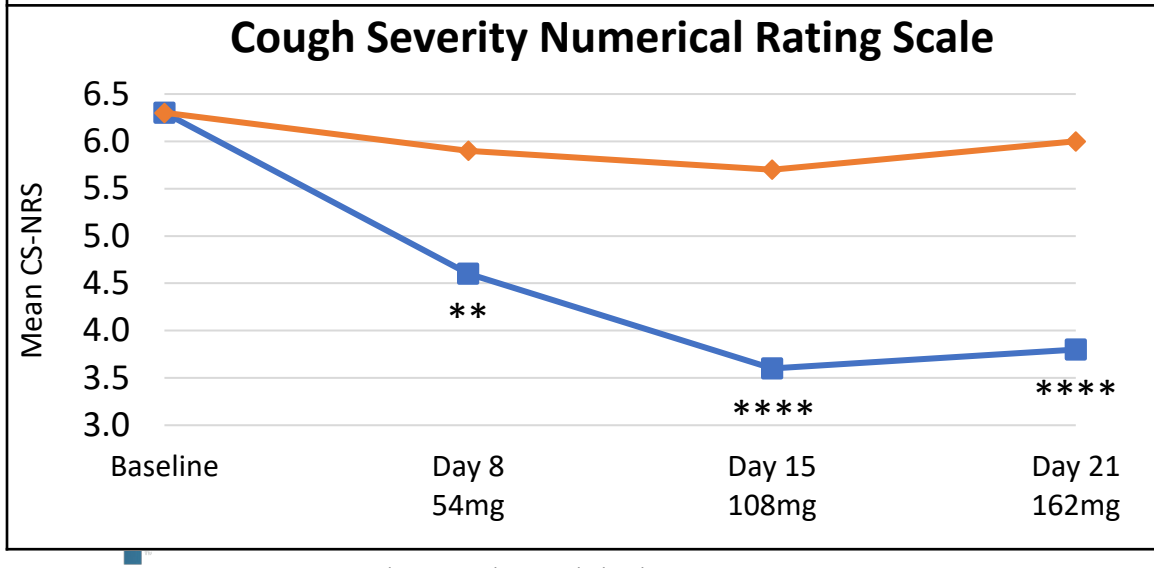


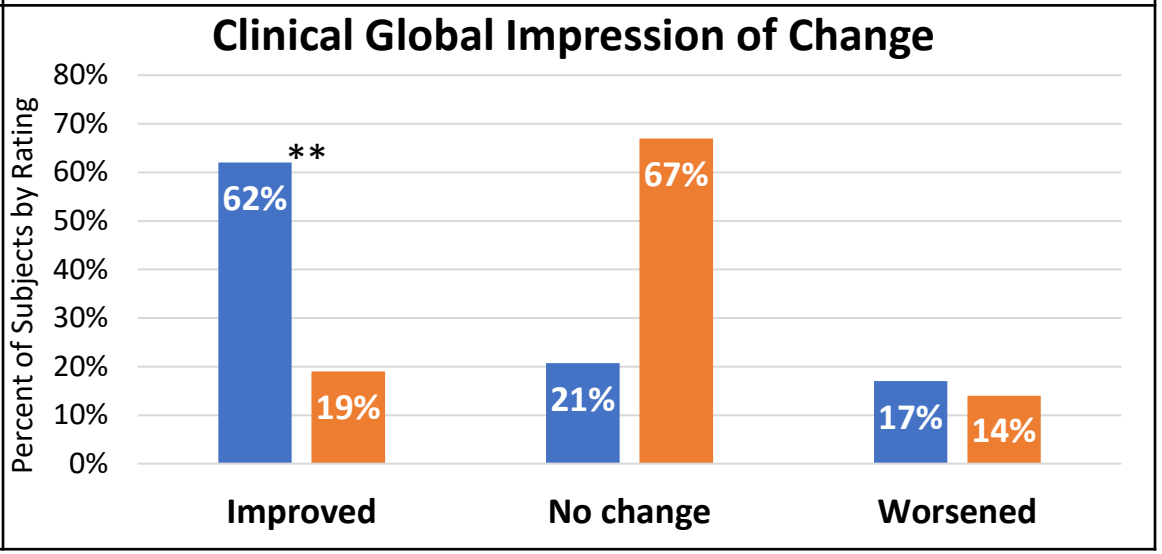
[1]Nguyen AM et al. J Allergy and Clin Immunol 2019 doi.org/10.1016/j.jaci.2018.12.519
Endpoint calculated as geometric mean percent change in 24Hr cough frequency from study baseline
Haduvio (nalbuphine ER) is an investigational drug

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

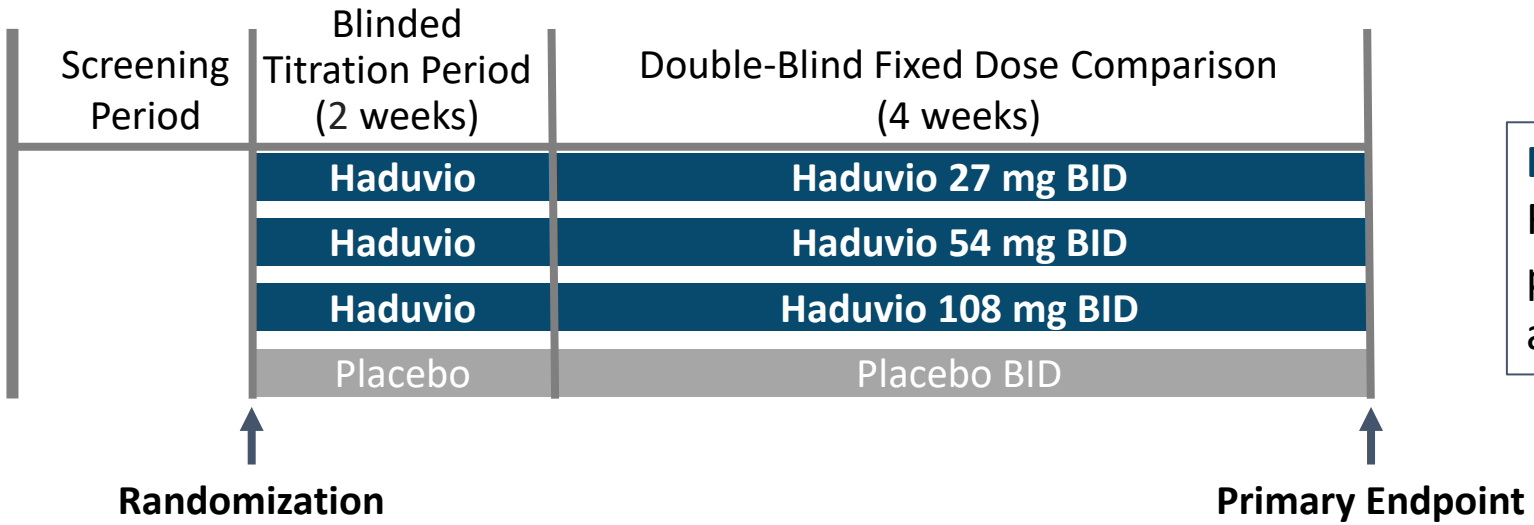
*p≤0.05 **p≤0.01 ***p≤0.001 ****p≤0.0001

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

	Haduvio BID 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

IPF Chronic Cough Dose Ranging Ph2b Trial Design (N ~200)



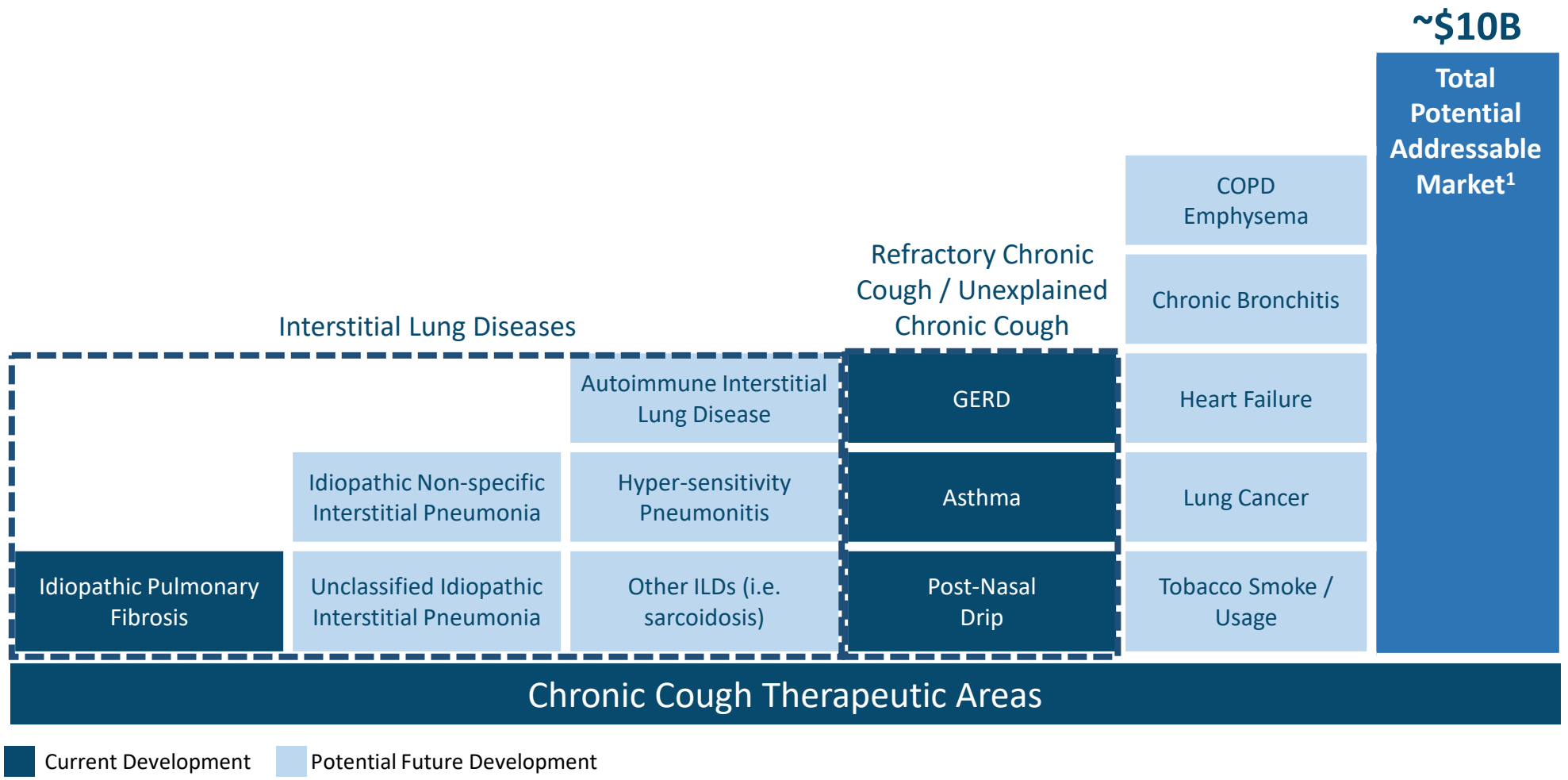
Design
Randomized, double-blind, placebo-controlled, parallel-arm design

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

Secondary Endpoints:
- Chronic Cough PROs

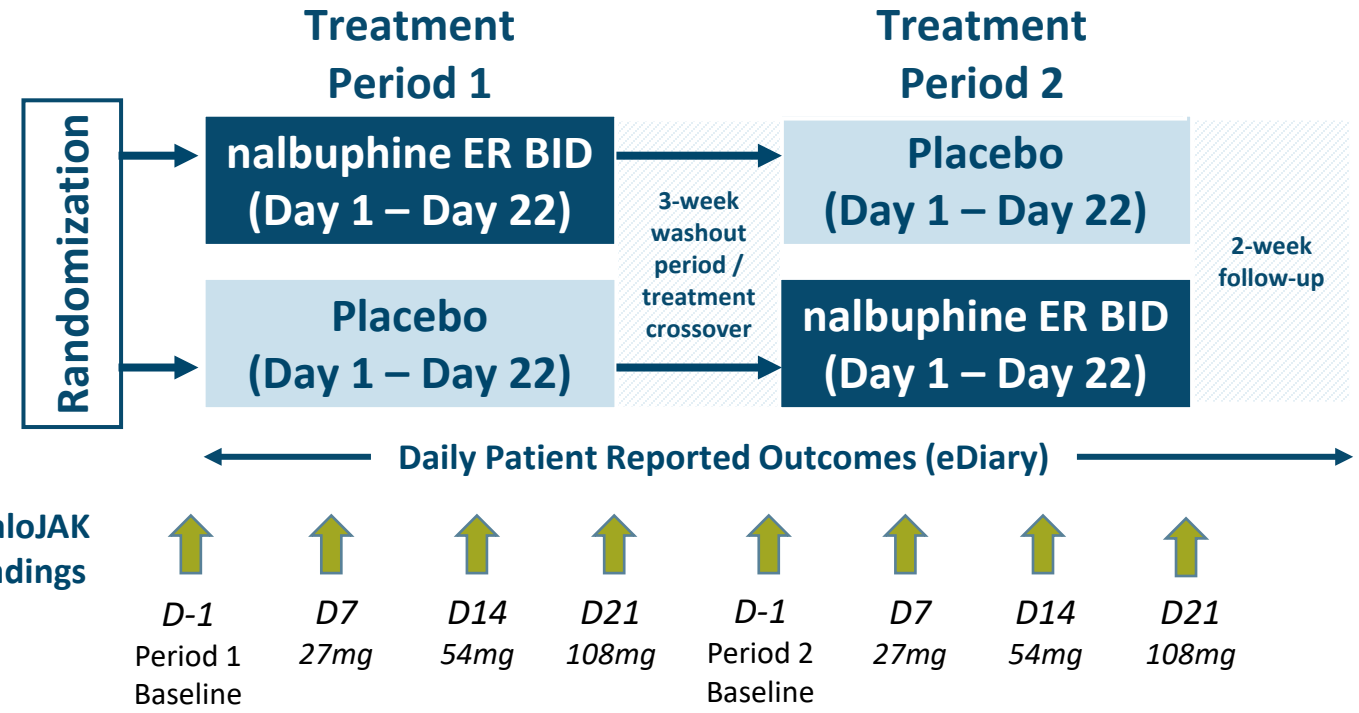
Design plan subject to discussions with regulatory authorities
Haduvio (nalbuphine ER) is an investigational drug

Opportunities in Chronic Cough



[1]2027 est. The Insight Partners Jun 2020

Refractory Chronic Cough Ph2 Trial Design (N ~60)



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

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

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

Design plan subject to discussions with regulatory authorities
Haduvio (nalbuphine ER) is an investigational drug

Clinical Need for Chronic Cough
Therapies and Mechanisms of Interest

Dr. Peter Dicpinigaitis, MD

Professor of Medicine, Albert Einstein College of Medicine
Division of Critical Care Medicine
Montefiore Medical Center
Director, Montefiore Cough Center
Editor-in-Chief, LUNG

Montefiore

EINSTEIN

Albert Einstein College of Medicine

Significance of Cough

- Most common complaint for which outpatients in the US seek medical attention

Rui P, Okeyode T. National Ambulatory Medical Care Survey: 2016 National Summary Tables. Available from: https://www.cdc.gov/nchs/data/ahcd/namcs_summary/2016_namcs_web_tables.pdf.

Categorization of Cough by Duration

- Acute — < 3 weeks
  - acute viral upper respiratory tract infection
- Subacute — 3-8 weeks
  - post-viral
  - ?Bordetella pertussis
  - ?pre-chronic
- Chronic — > 8 weeks
  - postnasal drip syndrome (upper airway cough syndrome)
  - asthma
  - non-asthmatic eosinophilic bronchitis
  - gastroesophageal reflux disease (GERD)
  - ***IPF**

Etiologies of Chronic Cough

- Nonsmoker, not on ACE inhibitor, normal/stable CXR

Upper Airway Cough Syndrome (PNDS; rhinitis)

asthma
non-asthmatic eosinophilic bronchitis

GERD (LPR)

Treatment of Chronic Cough

Diagnostic-Therapeutic Trials

Upper Airway Cough Syndrome; PNDS; rhinitis

- oral 1st-generation antihistamine
- inhaled corticosteroids
- inhaled ipratropium

Asthma; non-asthmatic eosinophilic bronchitis

- oral steroids
- inhaled steroids
- LTRAs

GERD (acid- and non-acid; liquid/gaseous components)

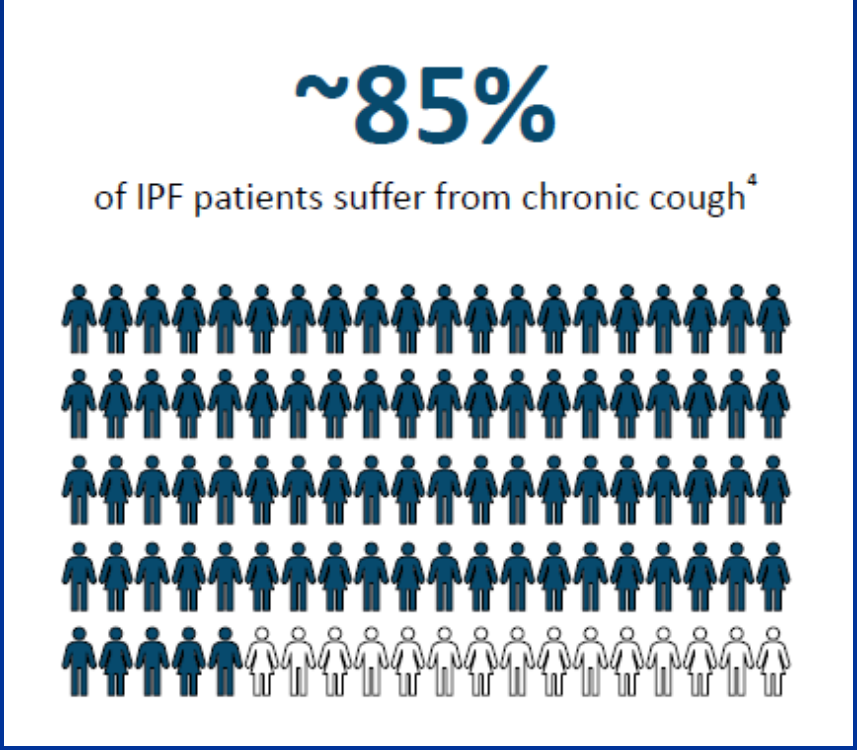
- acid-suppression therapy (high-dose PPI)
- anti-reflux lifestyle measures
- pro-kinetic agent (metoclopramide)

What if all empiric drug trials fail?

Refractory Chronic Cough

- A chronic cough that is not responsive to *appropriate and adequate* courses of therapy aimed at UACS, asthma/NAEB and reflux

Cough in IPF: a great burden and significant unmet need



Ryerson CJ et al. Respirology 2011

- Cough in IPF causes and/or exacerbates:
  - shortness of breath
  - fatigue
  - musculoskeletal pain
  - social isolation
  - urinary incontinence
- In ILD cough-specific QOL associated independently with hospitalization, death and lung transplantation

CHEST, September 2022

Therapeutic Options for Refractory Chronic Cough

Therapeutic Options for Refractory Chronic Cough

- The last novel antitussive agent approved by the FDA was in the year ____

Therapeutic Options for Refractory Chronic Cough

- The last novel antitussive agent approved by the FDA was in the year

1958

Therapeutic Options for Refractory Chronic Cough

- The last novel antitussive agent approved by the FDA was in the year

1958

There has never been a drug approved for *chronic* cough in the United States

Therapeutic Options for Refractory Chronic Cough

- opioids (hydrocodone, codeine, morphine)

- amitriptyline
- gabapentin

- speech therapy

Therapeutic Options for Refractory Chronic Cough

- opioids (hydrocodone, codeine, morphine)

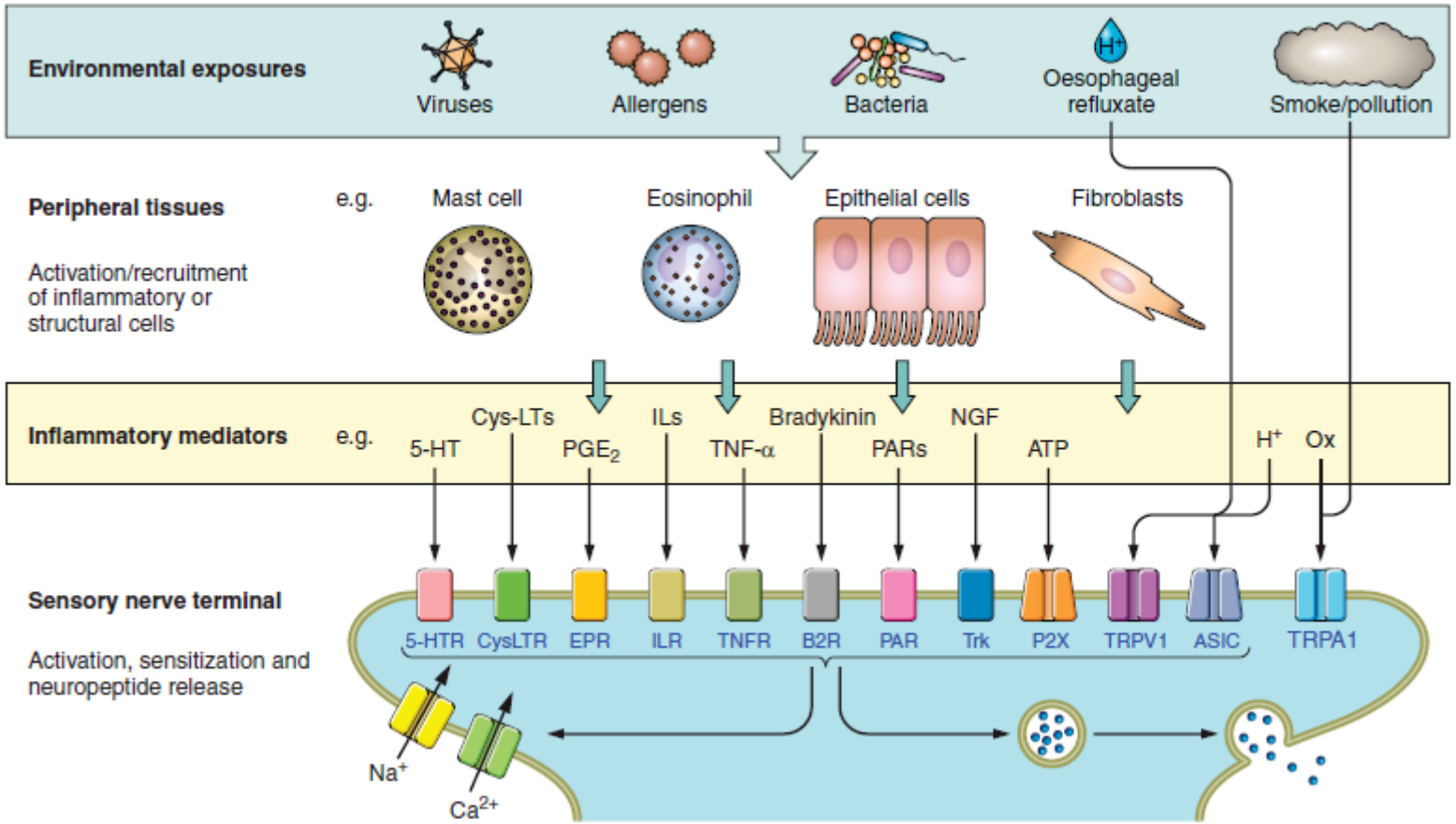
- amitriptyline
- gabapentin

- speech therapy
- **These often ineffective measures also used in the IPF-cough population, with similarly disappointing results**

Physiol Rev 96: 975–1024, 2016
Published June 8, 2016; doi:10.1152/physrev.00039.2015

VAGAL AFFERENT INNERVATION OF THE AIRWAYS IN HEALTH AND DISEASE

Stuart B. Mazzone and Bradley J. Undem



New Antitussive Drugs in the Research Pipeline

- TRPV1/TRPA1 antagonists
- P2X3 antagonists
- NK1 antagonists
- TRPM8 agonists
- Voltage-gated sodium-channel (NaV) blockers
- Ifenprodil – NMDA-receptor antagonist
- Opioid mu-antagonist/kappa agonist (nalbuphine ER)

New Antitussive Drugs in the Research Pipeline

- TRPV1/TRPA1 antagonists – multiple negative trials in TRPV1
- P2X3 antagonists – Phase 3 completed (Merck)
  Phase 3 initiated Jan, 2023 – Bellus
  Two programs discontinued: Bayer, Shionogi
- NK1 antagonists – IPF-cough only (NeRRe)
- TRPM8 agonists – Axalbion – Phase 2a completed
- Voltage-gated sodium-channel (NaV) blockers
  Nocion - Phase 2 (inhaled form only)
- Ifenprodil – +pilot study in IPF cough; Phase 2b in RCC planned
- Opioid mu-antagonist/kappa agonist (nalbuphine ER) – Phase 2b in IPF and RCC

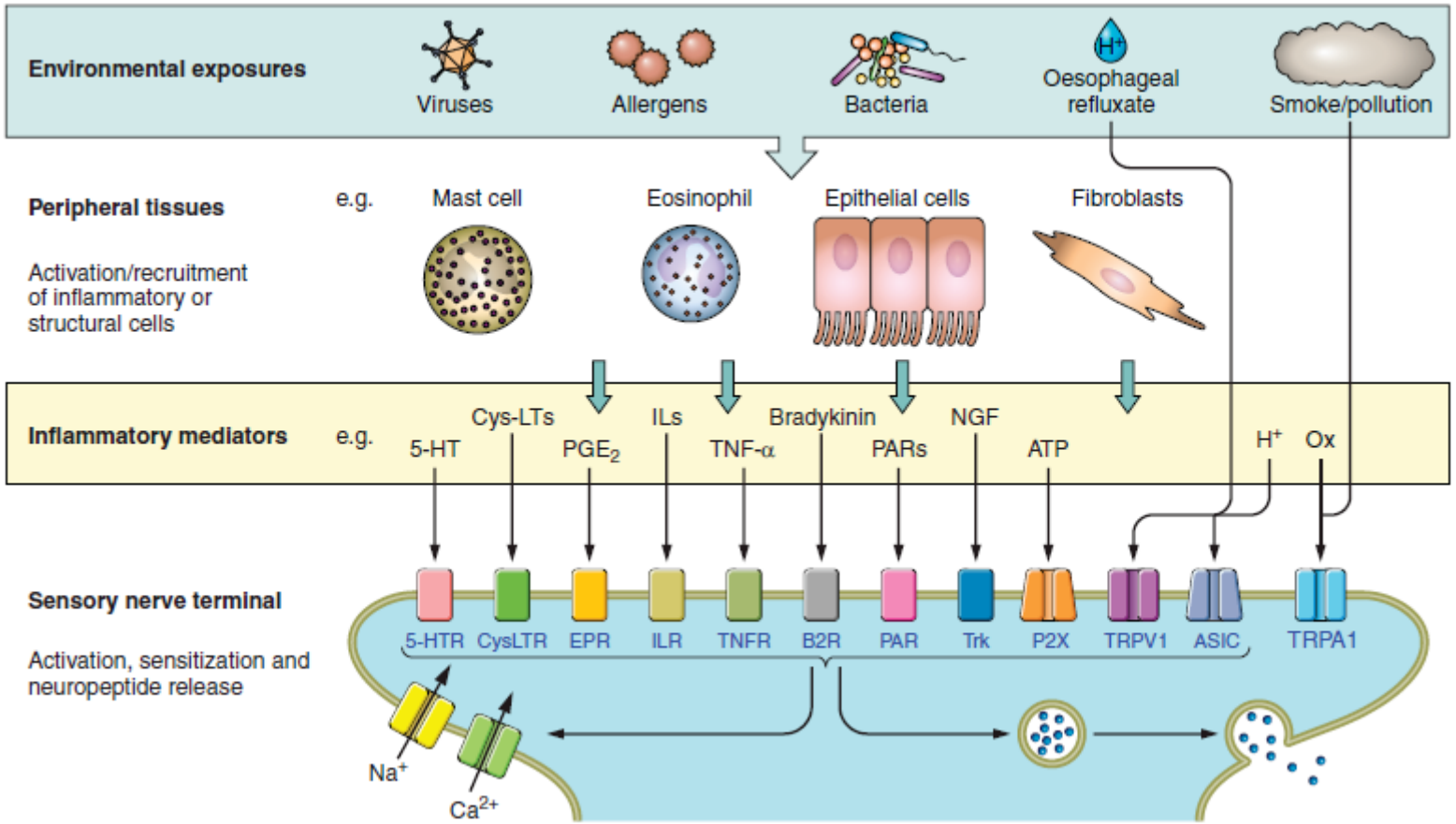
Central vs. Peripheral Mechanism

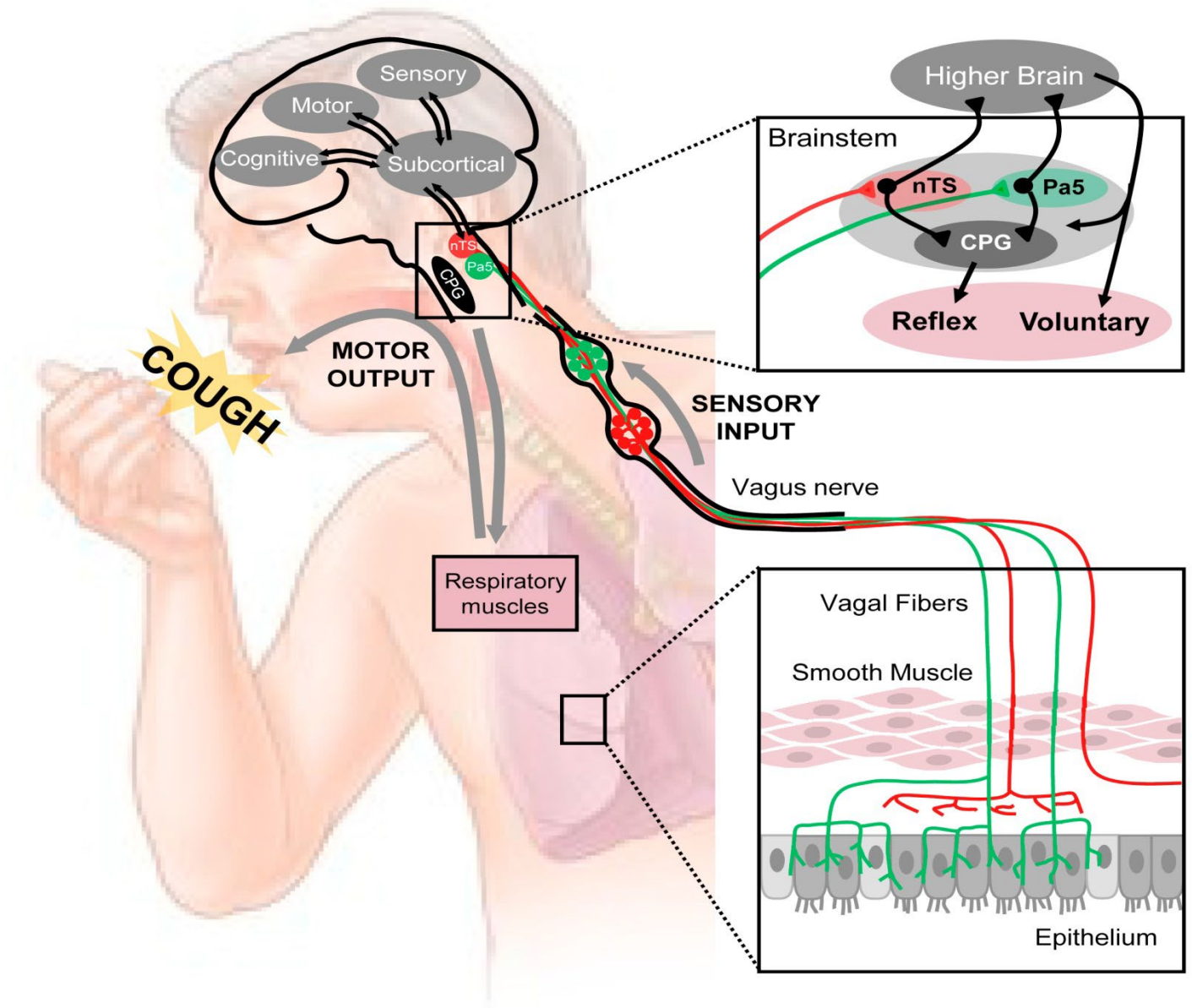
- Which is the ideal mechanism of action for an antitussive drug?

Physiol Rev 96: 975–1024, 2016
Published June 8, 2016; doi:10.1152/physrev.00039.2015

VAGAL AFFERENT INNERVATION OF THE AIRWAYS IN HEALTH AND DISEASE

Stuart B. Mazzone and Bradley J. Undem





Keller JA, et al. CHEST 2017;152:833-841

Central vs. Peripheral Mechanism

- Which is the ideal mechanism of action for an antitussive drug?

- **An effective *centrally-acting* drug will suppress cough *independent* of the initiating peripheral trigger in the airway**
- The effect of a *peripherally-acting* drug will be limited to suppression of cough that is induced by a specific peripheral trigger against which that drug is active

Central vs. Peripheral Mechanism

- Which is the ideal mechanism of action for an antitussive drug?
- An effective *centrally-acting* drug will suppress cough *independent* of the initiating peripheral trigger in the airway
- The effect of a *peripherally-acting* drug will be limited to suppression of cough that is induced by a specific peripheral trigger against which that drug is active
- **To date, centrally-acting drugs used for cough suppression have demonstrated inadequate efficacy and/or intolerable degrees of sedation and other side effects/issues (mu-opioid agonists; neuromodulators: amitriptyline, gabapentin)**

Peripherally-acting drugs have failed in clinical trials of IPF-associated cough

Pulm Ther (2021) 7:471–486
https://doi.org/10.1007/s41030-021-00162-9

Check for updates

ORIGINAL RESEARCH

Treatment of Persistent Cough in Subjects with Idiopathic Pulmonary Fibrosis (IPF) with Gefapixant, a P2X3 Antagonist, in a Randomized, Placebo-Controlled Clinical Trial

Fernando J. Martinez · Amna Sadaf Afzal · Jaclyn A. Smith · Anthony P. Ford · Jerry Jing Li · Yuping Li · Michael M. Kitt on behalf of the Chronic Cough in IPF Study Group

Phase 2B Study of Inhaled RVT-1601 for Chronic Cough in Idiopathic Pulmonary Fibrosis

A Multicenter, Randomized, Placebo-controlled Study (SCENIC Trial)

Fernando J. Martinez[1], Marlies S. Wijsenbeek[2], Ganesh Raghu[3,4], Kevin R. Flaherty[5], Toby M. Maher[6,7,8], Wim A. Wuyts[9], Michael Kreuter[10,11], Martin Kolb[12], Daniel C. Chambers[13,14], Charles Fogarty[15], Nesrin Mogulkoc[16], Ahmet S. Tutuncu[17], and Luca Richeldi[18]

Am J Respir Crit Care Med 2022;205:1084-1092

Future Therapeutic Landscape and Potential Implications of CANAL Trial Results

- Unmet need:

  great unmet need in IPF/ILD cough

  patients with RCC >>> IPF/ILD cough

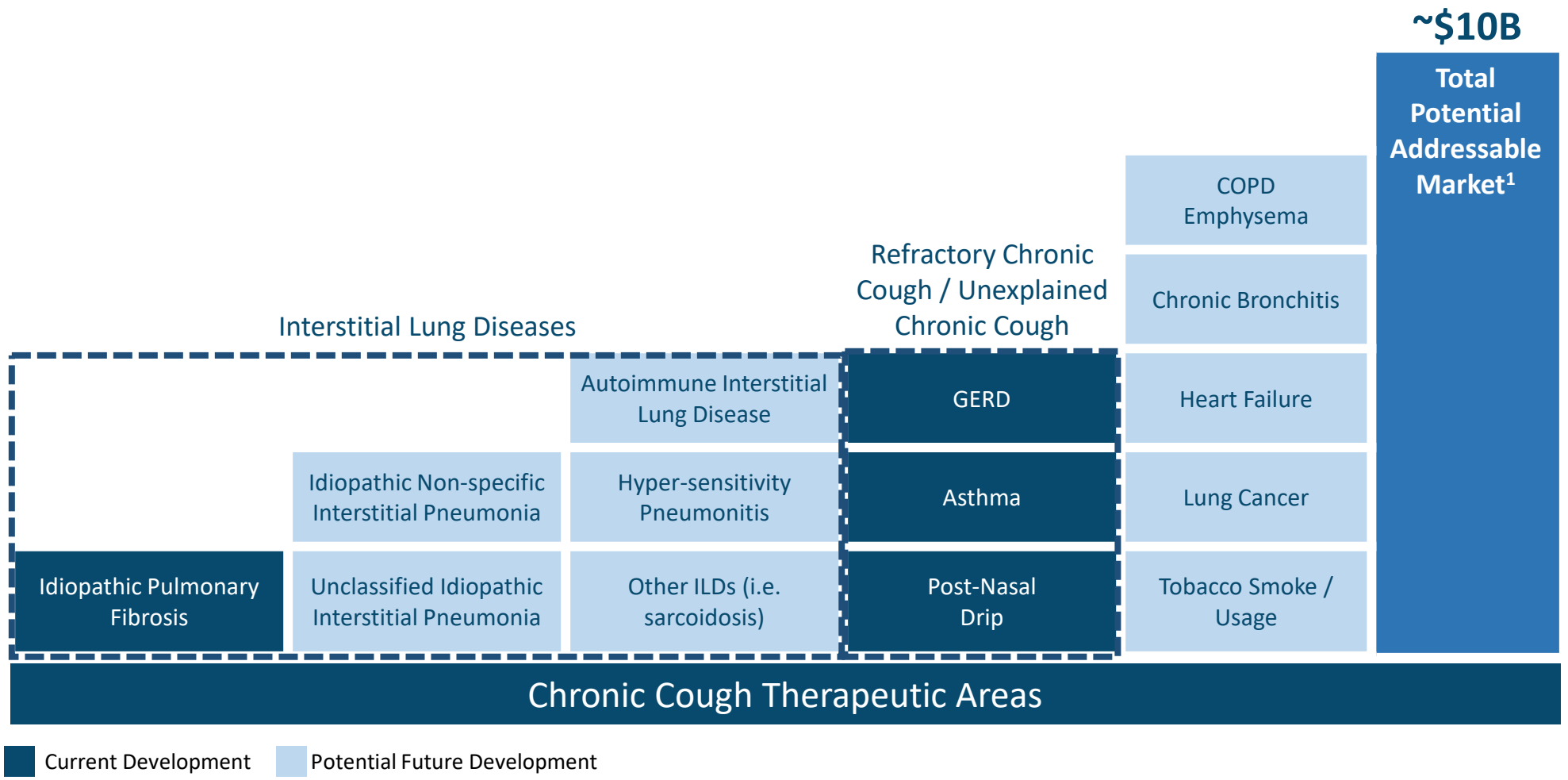
- Initial CANAL data support nalbuphine ER to be studied in RCC and other types of cough

Unmet Patient Need in Chronic Cough and Commercial Potential of Haduvio

Farrell Simon
Chief Commercial Officer

trevi™ THERAPEUTICS

Opportunities in Chronic Cough



[1]2027 est. The Insight Partners Jun 2020

Physicians Perceive Very High Unmet Need, Impact on QoL, and Urgency to Treat Patients Across All Types of Chronic Cough

Very Low 1 2 3 4 5 6 7 8 9 10 *Very High*

Unmet need in treating chronic cough in…

Impact on QoL for patients with chronic cough in…

Importance in treating patients with chronic cough in…

% of physicians

Bottom 3 boxes (1, 2, 3) **Middle 4 boxes (4, 5, 6, 7)** **Top 3 boxes (8, 9, 10)**

Source: Interviews and quantitative study conducted by Indegene, 2022 with US pulmonologists, ILD specialists, and general practitioners (n = 105)
Based on Pulmonologists who managed IPF patients with chronic cough in the last 12 months
Based on Pulmonologists who managed Non IPF PF-ILD patients with chronic cough in the last 12 months
PF-ILD: Progressive Fibrotic-Interstitial Lung Disease; RCC: Refractory Chronic Cough

Competitive Landscape
Chronic Cough Has an Opportunity for Additional Mechanisms of Action

Chronic Cough in Idiopathic Pulmonary Fibrosis (IPF)

	Mechanism	Current Stage	VitaloJAK® Results (PBO Adj Chg.)	
Haduvio[1]	**kappa agonist + mu antagonist**	**Ph2**	**Ph2: 52.5% (p<0.0001)**	✓
orvepitant[2]	NK1 antagonist	Ph2	TBD	
gefapixant[3]	P2x3i	Terminated (Efficacy)	Ph2: 5% NS	✗
RVT-1601[4]	Cromolyn sodium	Terminated (Efficacy)	Ph2: 0% NS	✗

Refractory Chronic Cough (RCC)

	Mechanism	Current Stage	VitaloJAK® Results (PBO Adj Chg.)	
Haduvio[5]	**kappa agonist + mu antagonist**	**Ph2**	**TBD**	
gefapixant[6]	P2x3i	Filing	Ph3: 15-18% (p=0.03)	✓
BLU-5937[7]	P2x3i	Ph3	Ph2: 34% (p≤0.005)	✓
sivopixant[8]	P2x3i	Terminated (Efficacy)	Ph2: -12-13% NS	✗
eliapixant[9]	P2x3i	Terminated (Safety)	Ph2: 14-29 NS	✗
orvepitant[10]	NK1 antagonist	Terminated (Efficacy)	Ph2: NS	✗
serlopitant[11]	NK1 antagonist	Terminated (Efficacy)	Ph2: NS	✗

trevi THERAPEUTICS

[1]Molyneaux P. et al. *Thorax* 2022;77:A13-A14. http://dx.doi.org/10.1136/thorax-2022-BTSabstracts.21 [2]https://clinicaltrials.gov/ct2/show/NCT02993822 [3]Martinez FJ et al. Pulm Ther. 2021 Dec;7(2):471-486. doi: 10.1007/s41030-021-00162-9 [4]Martinez FJ et al. Am J Respir Crit Care Med. 2022 May 1;205(9):1084-1092. doi: 10.1164/rccm.202106-1485OC [5]Trevi Therapeutics Press Release January 5, 2023 [6]McGarvey LP et al. Lancet. 2022 Mar 5;399(10328):909-923. doi: 10.1016/S0140-6736(21)02348-5 [7]Bellus Health Press Release December 13, 2021 [8]McGarvey L et al. Lung. 2022 Dec 13:1–11. doi: 10.1007/s00408-022-00592-5 [9]Dicpinigaitis P et al. Am J Respir Crit Care Med 2022;205:A4776 https://doi.org/10.1164/ajrccm-conference.2022.205.1_MeetingAbstracts.A4776 [10]Nerre Therapeutics Press Release June 7, 2019 [11]Menlo Press Release Oct 08, 2018

Haduvio (nalbuphine ER) is an investigational drug. VitaloJAK is a registered trademark of VitaloGraph. NS = Not Significant

Haduvio Has Broad Market Potential in Difficult to Treat Chronic Cough Patients

IPF[1]
~140k US patients

Haduvio eligible moderate-severe cough (~100k patients)[2]

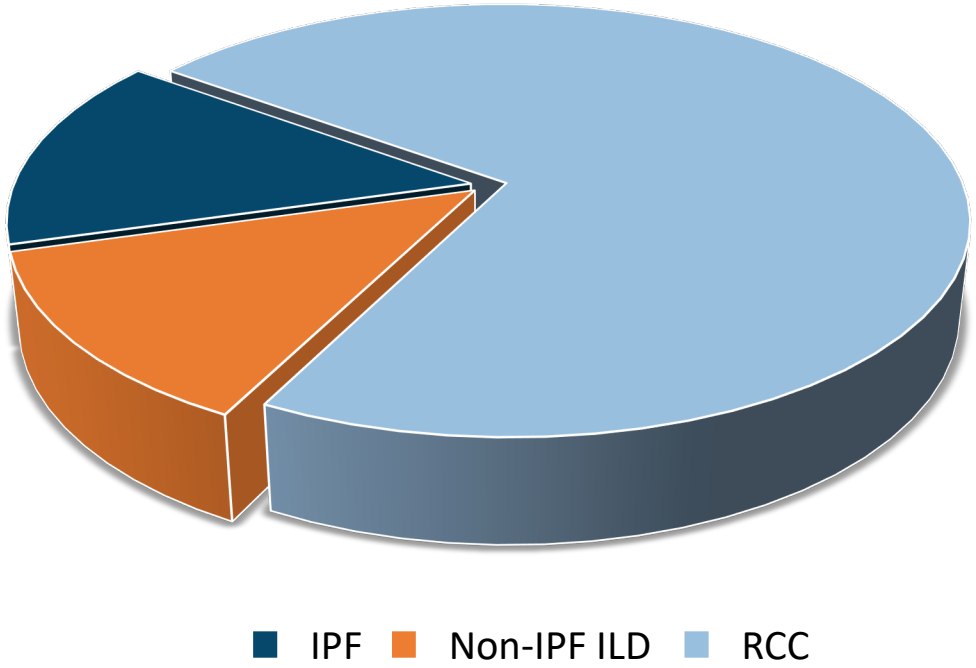
Mild to no cough (~40k patients)

Non-IPF ILD[3]
~140k US patients

Haduvio eligible moderate-severe cough (~90k patients)[4]

Mild to no cough (~50k patients)

US Market Opportunity for Haduvio
~700k Chronic Cough Patients



Refractory Chronic Cough
~1.8M US patients[5,6]

Haduvio eligible severe cough (~250-350k patients)[6]

Haduvio eligible P2x3 failures (~150-250k patients)[6]

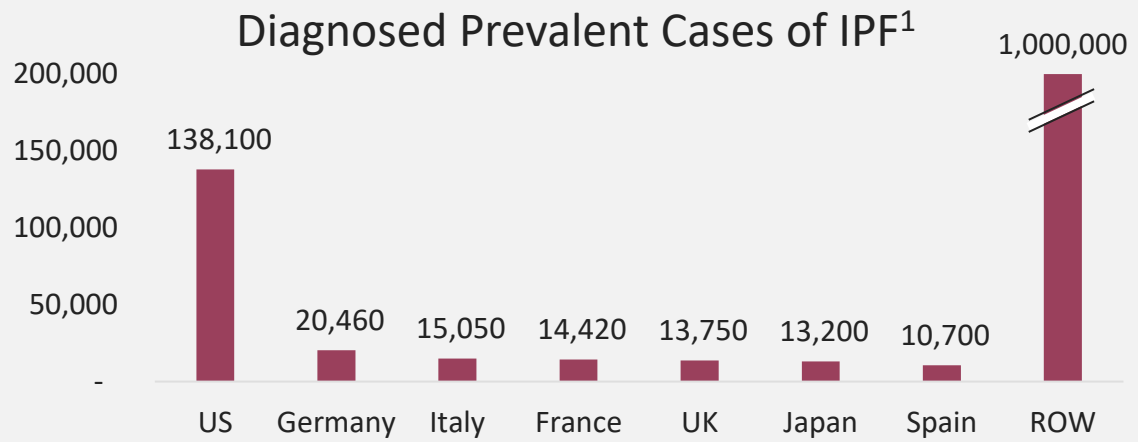
Mild cough (~250k patients)[6]

Moderate cough adequately controlled (~740k patients) [6]

[1]Datamonitor 2015 Idiopathic Pulmonary Fibrosis Disease Coverage Ref Code: DMKC12770 [2]Indegene/Trevi Therapeutics Market Research (2022) N = 100 US Pulmonologists [3]Kaul B et al. Front Med 2021 doi.org/10.3389/fmed.2021.751181
[4]Indegene/Trevi Therapeutics Market Research (2022) N = 30 US Pulmonologists [5]Meltzer EO et al. J All Clin Immun 2021 doi.org/10.1016/j.jaip.2021.07.022 [6]LifeSci Capital Report Dec 22, 2022

Prevalence and Significant Role of Chronic Cough in IPF

Epidemiology



30,000-40,000
Incident cases of IPF in the US every year[2]

Up to 1,500
coughs per day in an IPF patient.[3,4] The urge to cough cannot be relieved by coughing.[5]

Up to 85%
of IPF patients experience chronic cough[6]

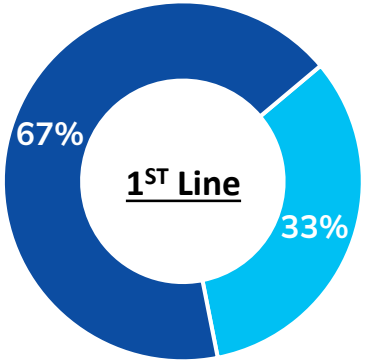
- **IPF is a high burden disease** that has a significant impact on QoL, e.g.:[3-8]
  - Coughing can increase feelings of anxiety as it induces breathlessness
  - Coughing spells or episodes lead to significant fatigue, air hunger, peripheral oxygen desaturation
  - The social impact and isolation of 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**[9]
- 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[6,10]

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

Physicians Currently Use Tessalon Perles and Proton-Pump Inhibitors (PPIs) for Managing Chronic Cough in IPF Patients

Results look similar across IPF, non-IPF ILDs and RCC

Solo Therapy
Combination Therapy
No Line prescribed (2nd or 3rd)

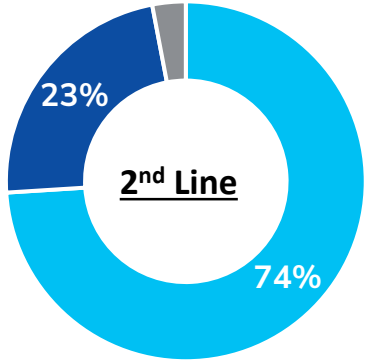


% of physicians

Majority of physicians are prescribing…

Tessalon Perles

- Tessalon Perles + PPIs

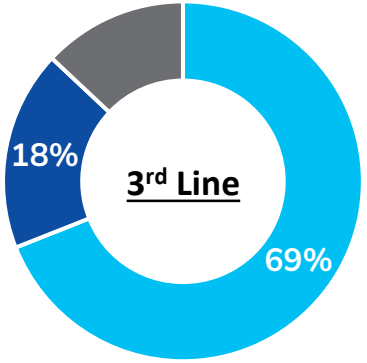


% of physicians

Majority of physicians are prescribing…

Neuromodulators (e.g. gabapentin)

- Tessalon Perles + Neuromodulators or PPIs or Codeine/Morphine



% of physicians

Majority of physicians are prescribing…

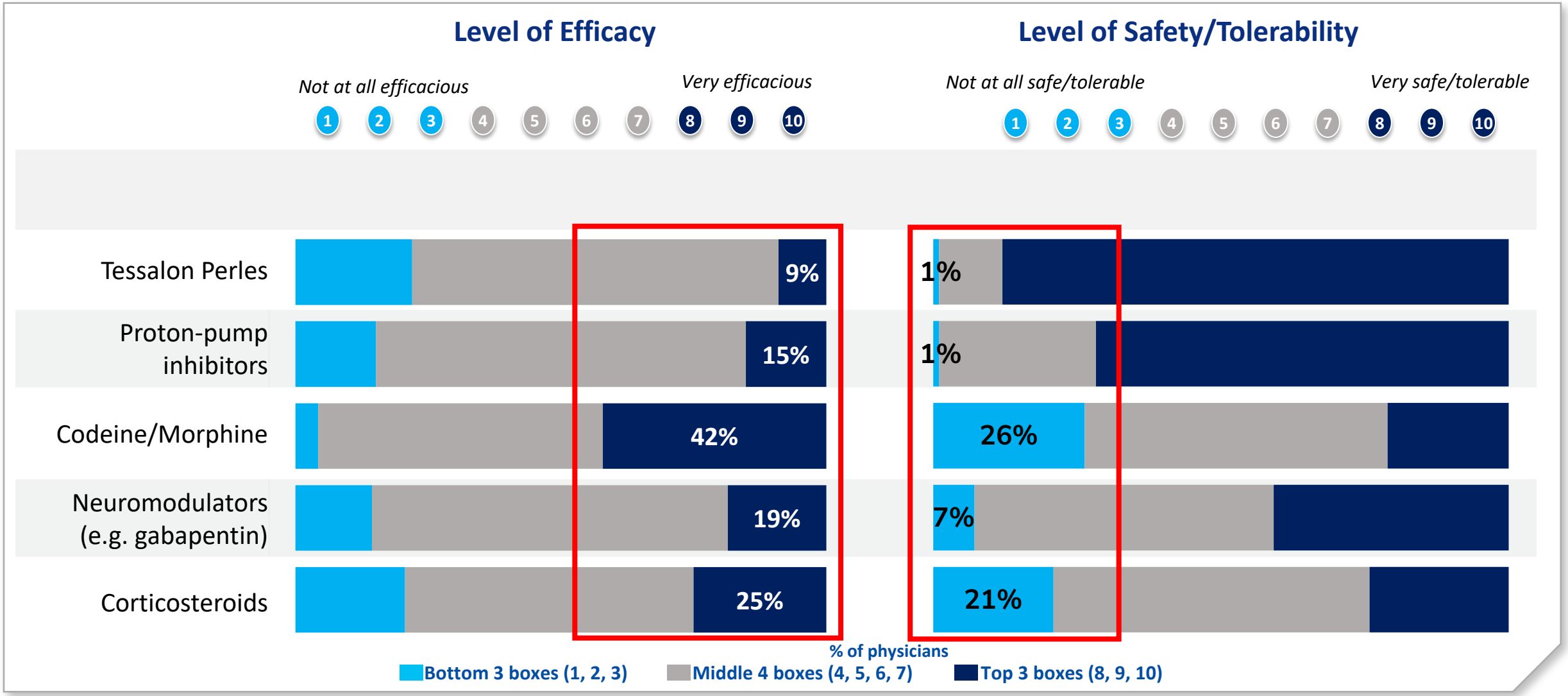
PPIs

- Tessalon Perles + Codeine/Morphine + Neuromodulators
- Tessalon Perles + Neuromodulators + PPIs
- Tessalon Perles + Codeine/Morphine + Neuromodulators + PPIs

Source: Interviews and quantitative study conducted by Indegene, 2022 with US pulmonologists (n = 100)
Based on physicians who prescribed IPF patients with chronic cough more than one cough therapy in the last 12 months.

(N=98)*

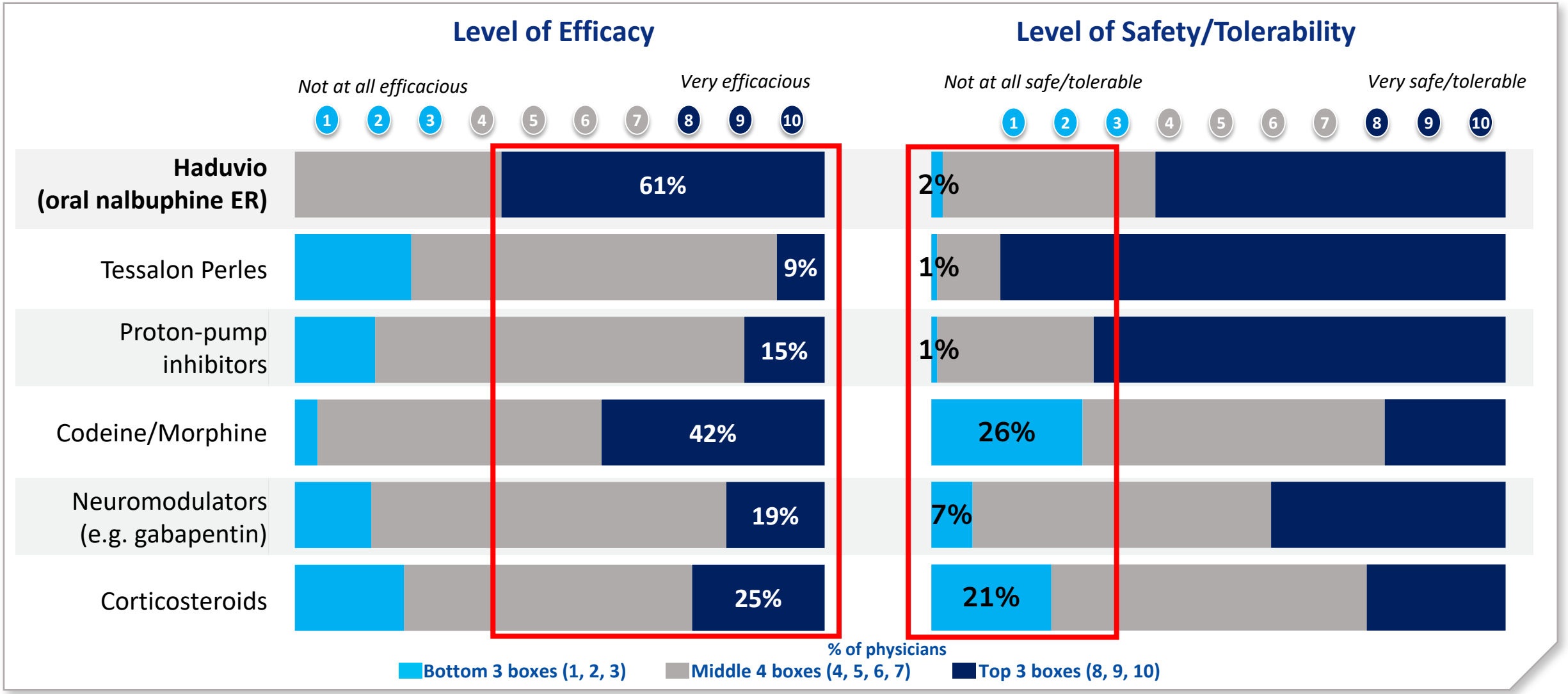
Off-Label Therapies are Perceived by Pulmonologists as Ineffective or Have Potential Safety/Tolerability Concerns



Source: Interviews and quantitative study conducted by Indegene, 2022 with US pulmonologists (n = 100)
Based on Target Product Profile of Haduvio
Haduvio (nalbuphine ER) is an investigational drug

(N=100)

Pulmonologists Perceive Haduvio as an Efficacious and Safe/Tolerable Therapy for Their IPF Patients with Chronic Cough

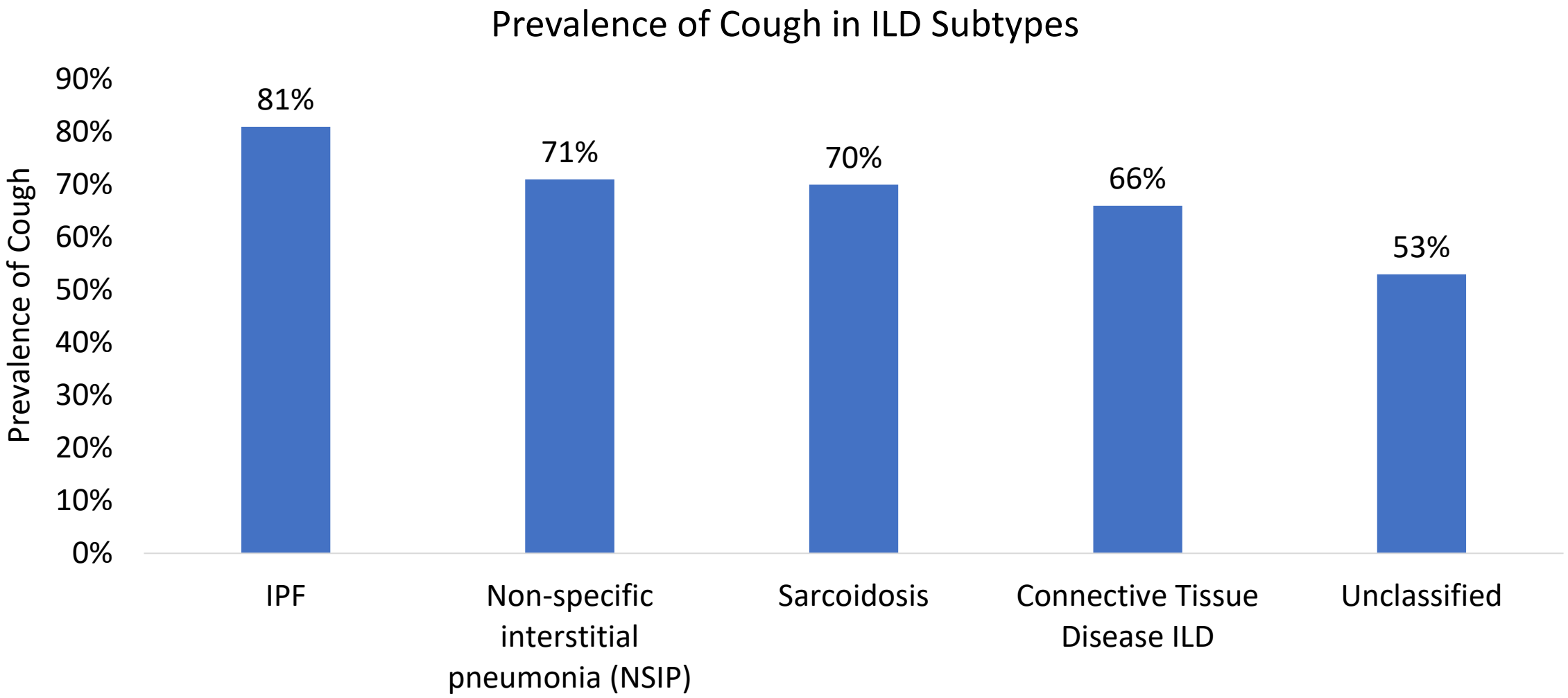


Source: Interviews and quantitative study conducted by Indegene, 2022 with US pulmonologists (n = 100)
Based on Target Product Profile of Haduvio
Haduvio (nalbuphine ER) is an investigational drug

(N=100)

Chronic Cough Also Has a High Prevalence in non-IPF ILDs

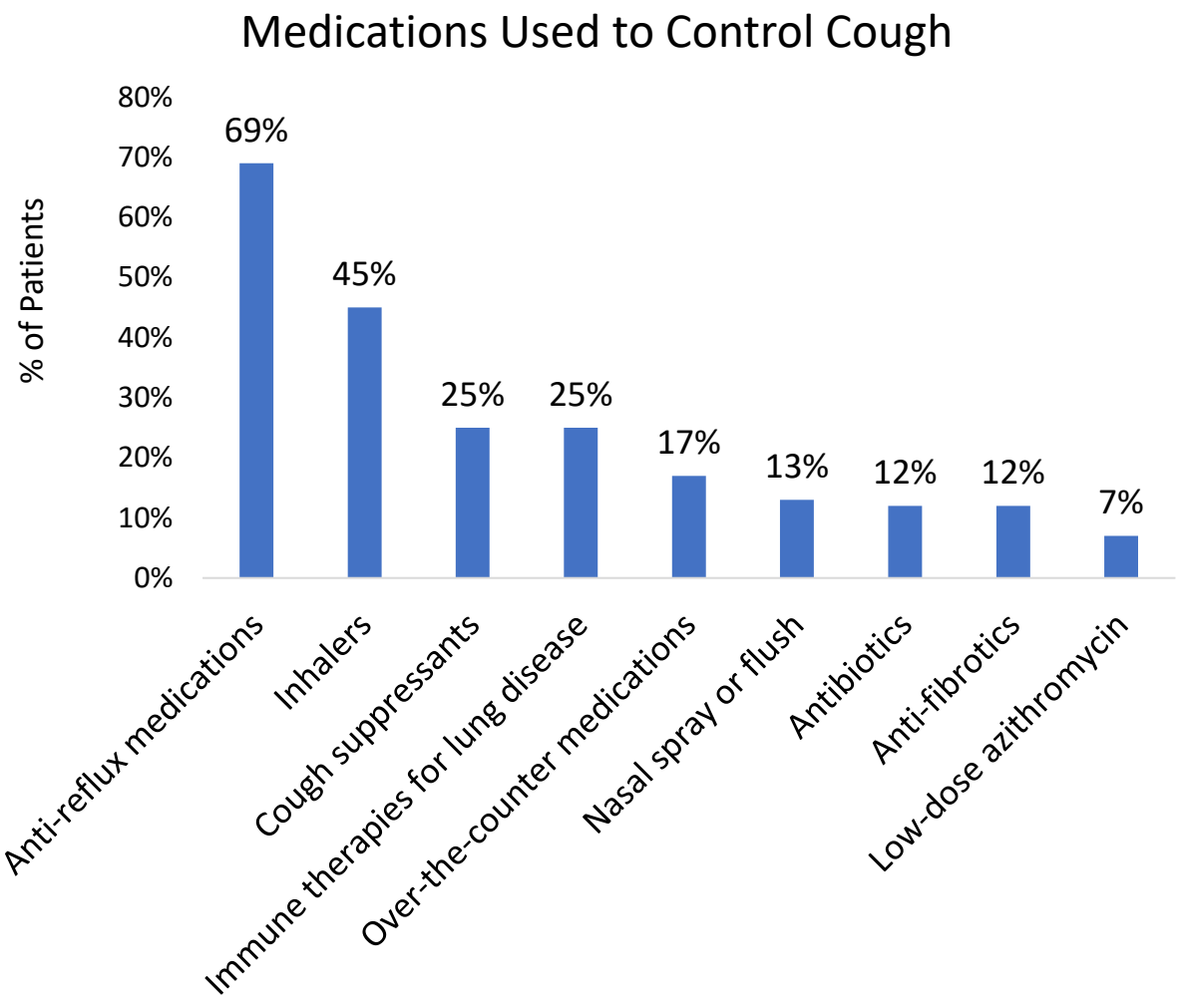
Non-IPF ILD
Chronic Cough

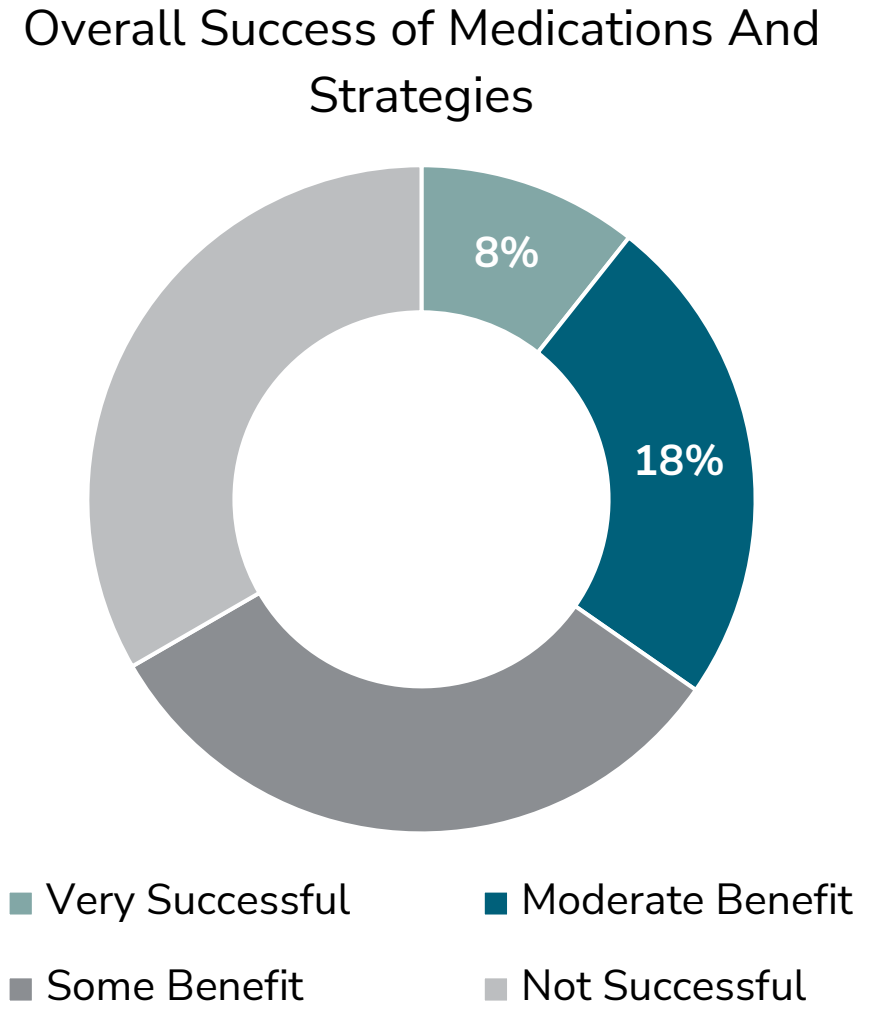


Lan, N.S.H., Moore, I. and Lake, F. (2021), Intern Med J, 51: 923-929. https://doi.org/10.1111/imj.14837

Management of Chronic Cough in Interstitial Lung Diseases (ILDs) Has Marginal Success

Non-IPF ILD
Chronic Cough





Lan, N.S.H., Moore, I. and Lake, F. (2021), Intern Med J, 51: 923-929. https://doi.org/10.1111/imj.14837

Pulmonologists Expect to Consider 63% Of Patients with non-IPF ILDs as Eligible for Haduvio, if Approved

Non-IPF ILD
Chronic Cough

Pulmonologists' reactions to potential future indication of Haduvio

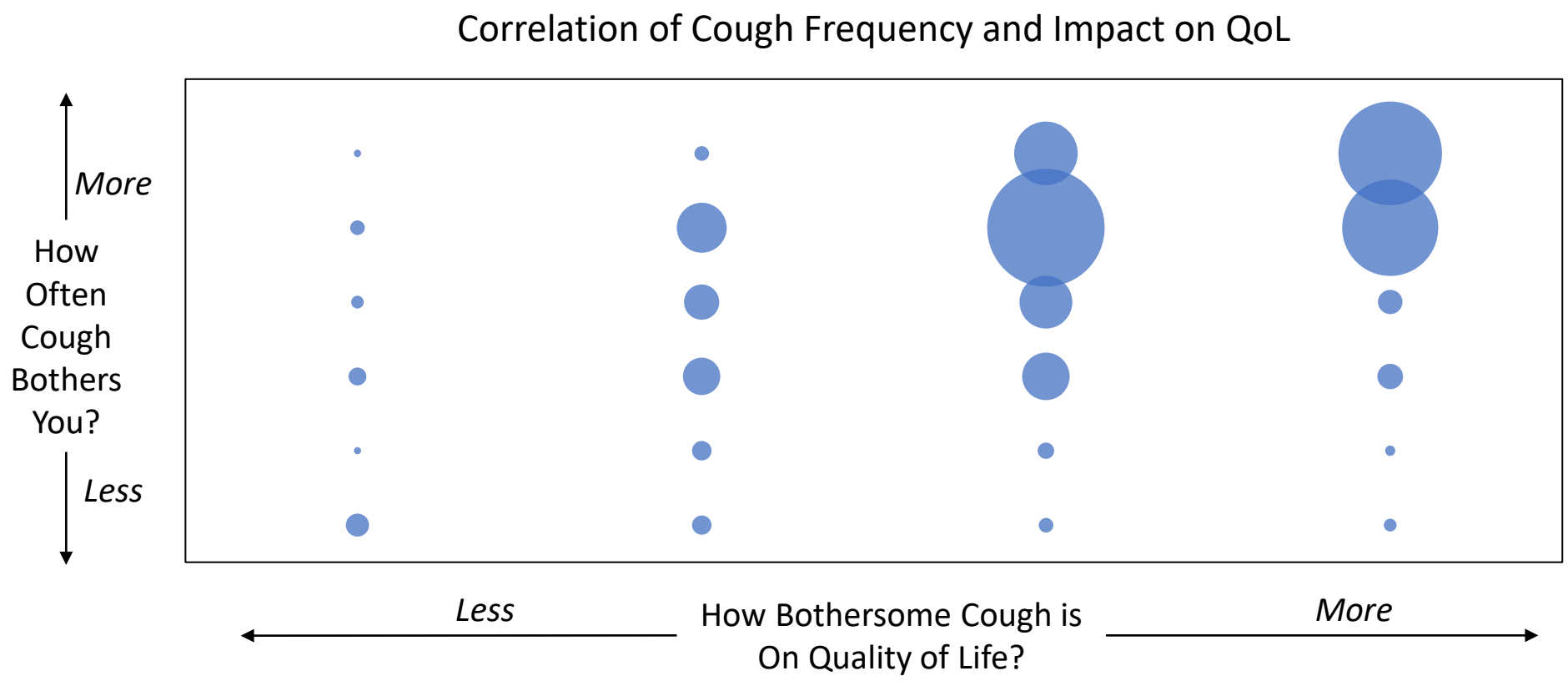
Disease Type	Avg. # of patients treated in the last 12 months	Avg. % of patients expected to be considered candidates for Haduvio
Non-IPF Interstitial Lung Diseases (ILDs)	64 patients (6% of overall practice patient population)	63% (N=100)

Source: Interviews and quantitative study conducted by Indegene, 2022 with US pulmonologists (n = 100)
Based on Target Product Profile of Haduvio
Haduvio (nalbuphine ER) is an investigational drug

(N=100)

Refractory Chronic Cough (RCC) Patients Have a High Frequency of Bothersome Cough Impacting Quality of Life (QoL)

Refractory chronic cough patients are most bothered by their cough when it occurs frequently

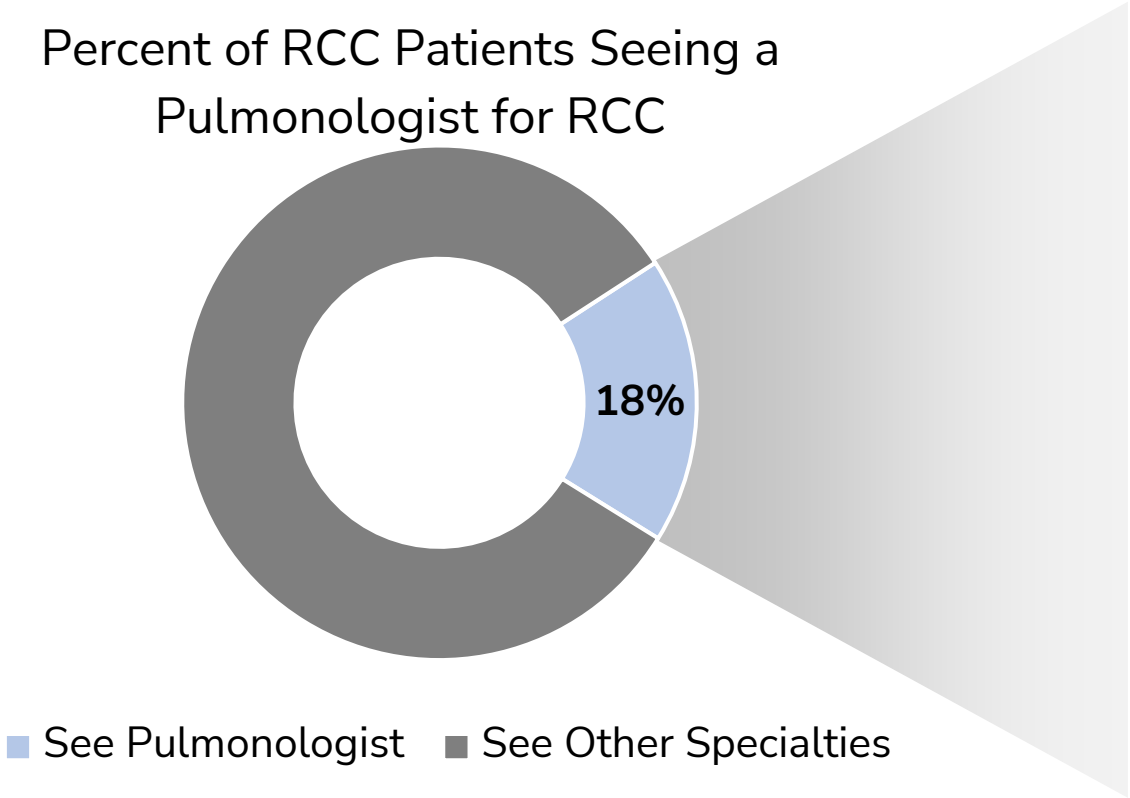


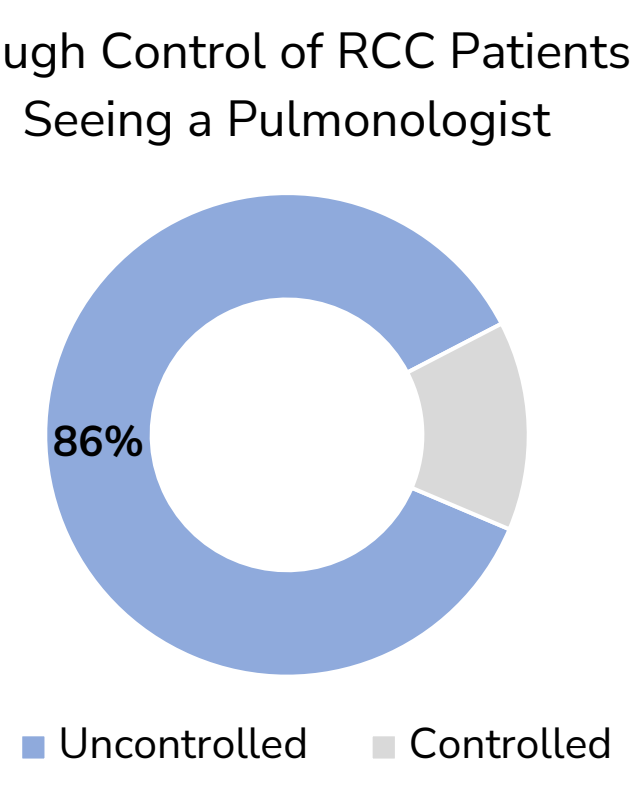
"How often did or does your cough typically bother you?"
"How bothersome is or was your cough on your quality of life?"
LifeSci Capital Report Nov 2022 (N=1,000)

(N=1000)

RCC Patients Seeing a Pulmonologist Remain Uncontrolled

86% of RCC patients seeing a Pulmonologist are uncontrolled on current therapies





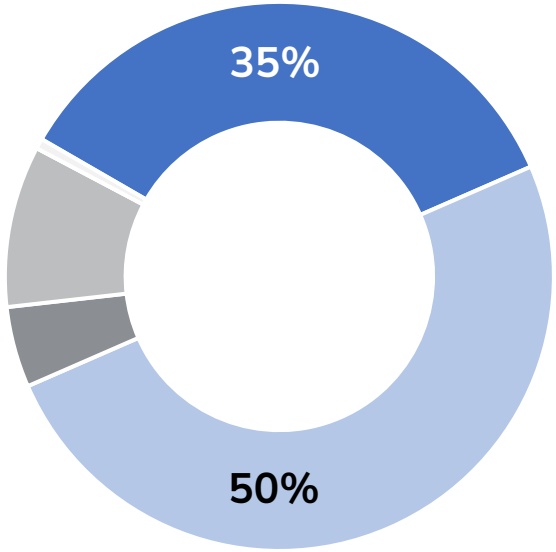
Have you ever sought medical care for your cough from any of the following? Pulmonologist
Have you had a cough that has lasted for more than 8 weeks and has persisted despite treatment?
LifeSci Capital Report Nov 2022 (N=1,000)

(N=1000)

RCC Patients Seeing a Pulmonologist Have a High Frequency of Cough and Experience a Significant Impact on Their Quality of Life (QoL)

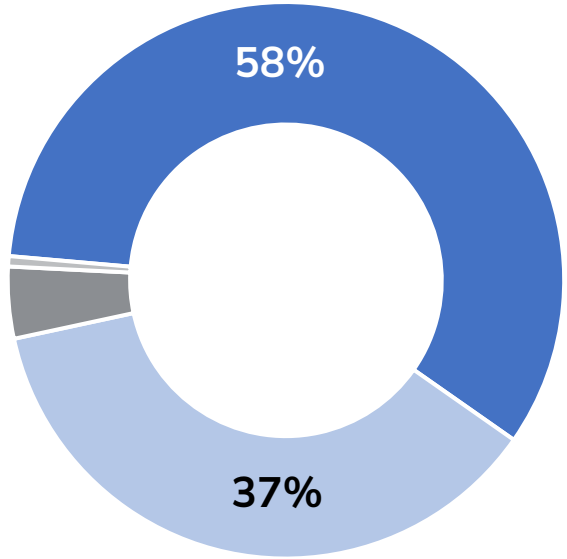
A majority of refractory chronic cough patients are bothered by cough daily and find it somewhat to very bothersome

Frequency of Chronic Cough in RCC Patients Seeing a Pulmonologist



- Constantly
- Several Times Per Day
- 1/Day
- Several Times Per Week
- 1/Week
- <1/Week

Impact of Chronic Cough on QoL in RCC Patients Seeing a Pulmonologist



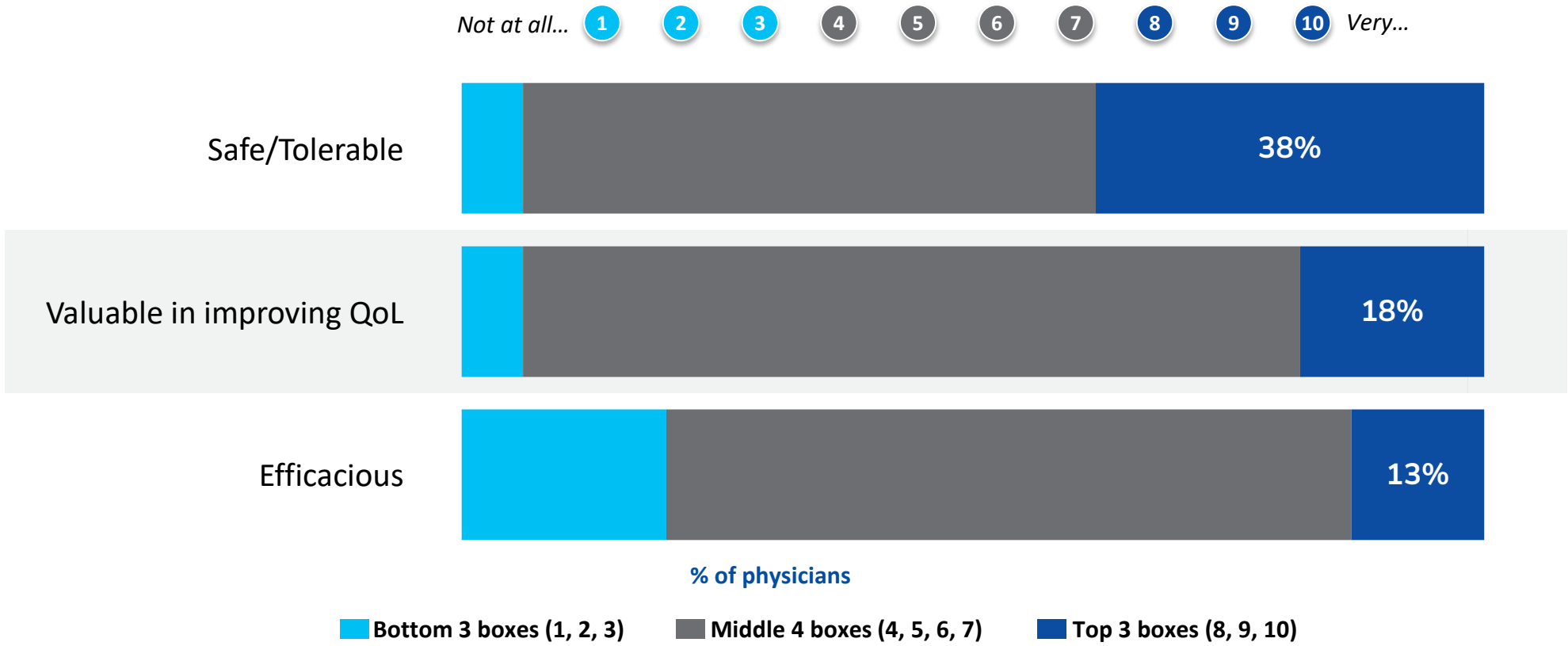
- Very Bothersome
- Somewhat Bothersome
- Not Too Bothersome
- Not Bothersome At All

"How often did or does your cough typically bother you?"
"How bothersome is or was your cough on your quality of life?"
LifeSci Capital Report Nov 2022 Patients Treated By a Pulmonologist (N=168)

(N=168)

Current Off-Label Therapies Are Not Seen by Pulmonologists as Valuable or Efficacious

Current treatments level of efficacy, safety and value in improving QoL by reducing chronic cough in RCC



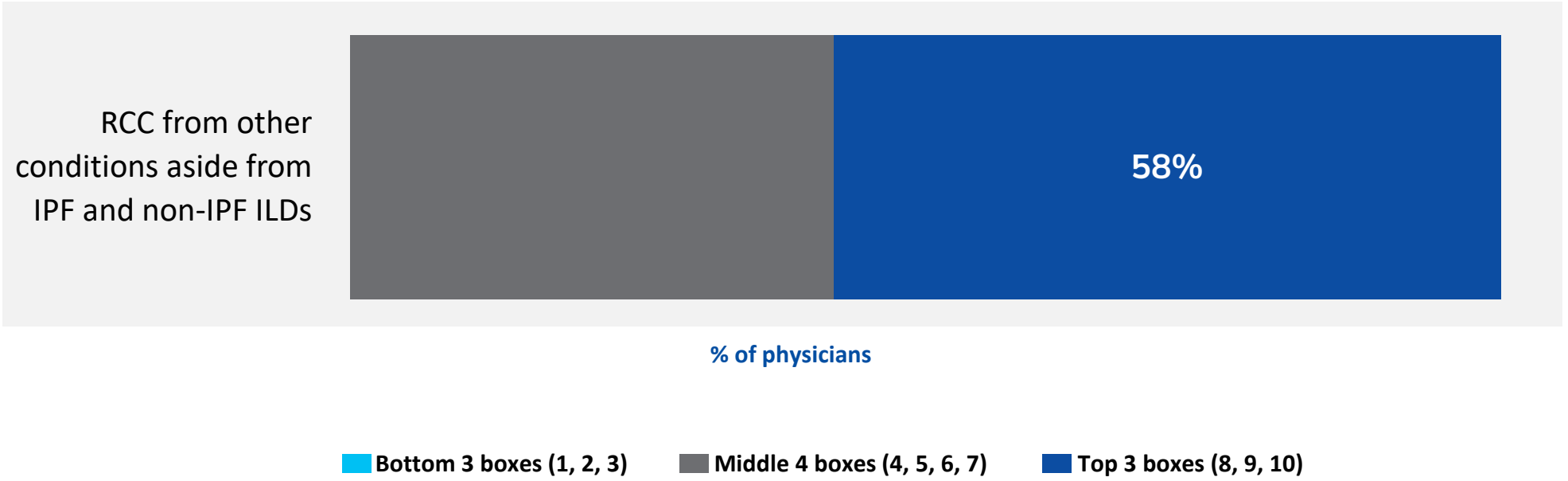
Source: Interviews and quantitative study conducted by Indegene, 2022 with US pulmonologists (n = 30) and PCPs (N=15)

(N=45)

Physicians View Haduvio as a Potential Therapy for a Majority of RCC Patients, Based on the Target Product Profile

Likelihood to prescribe Haduvio to patients with…

Not at all likely to prescribe Haduvio 1 2 3 4 5 6 7 8 9 10 *Very likely to prescribe Haduvio*



Source: Interviews and quantitative study conducted by Indegene, 2022 with US pulmonologists (n = 30) and PCPs (N=15)
Haduvio (nalbuphine ER) is an investigational drug

(N=45)

Broad Market Potential of Haduvio in Difficult to Treat Chronic Cough Patients

IPF[1]
~140k US patients

Haduvio eligible moderate-severe cough (~100k patients)[2]

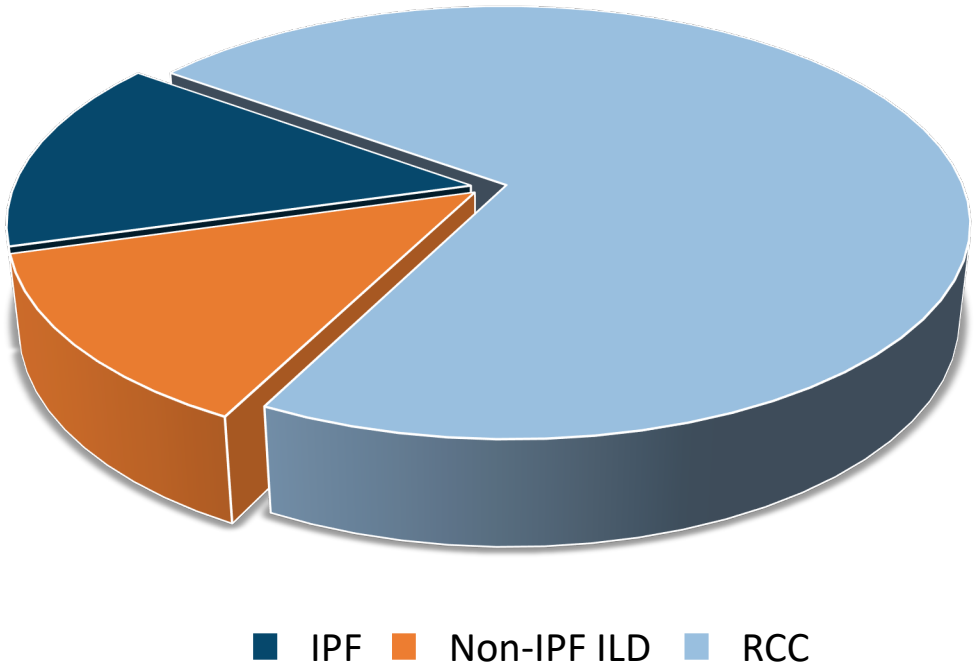
Mild to no cough (~40k patients)

Non-IPF ILD[3]
~140k US patients

Haduvio eligible moderate-severe cough (~90k patients)[4]

Mild to no cough (~50k patients)

US Market Opportunity for Haduvio
~700k Chronic Cough Patients



Refractory Chronic Cough
~1.8M US patients[5,6]

Haduvio eligible severe cough (~250-350k patients)[6]

Haduvio eligible P2x3 failures (~150-250k patients)[6]

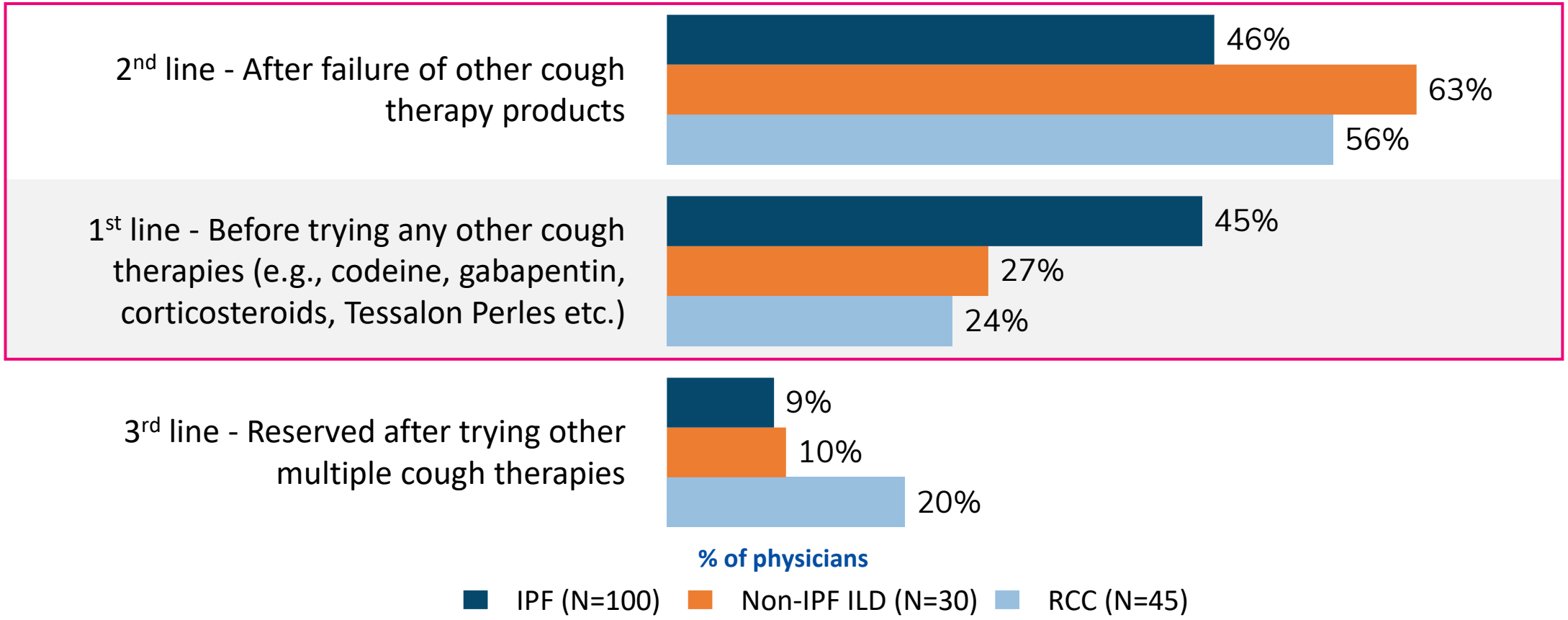
Mild cough (~250k patients)[6]

Moderate cough adequately controlled (~740k patients) [6]

[1]Datamonitor 2015 Idiopathic Pulmonary Fibrosis Disease Coverage Ref Code: DMKC12770 [2]Indegene/Trevi Therapeutics Market Research (2022) N = 100 US Pulmonologists [3]Kaul B et al. Front Med 2021 doi.org/10.3389/fmed.2021.751181
[4]Indegene/Trevi Therapeutics Market Research (2022) N = 30 US Pulmonologists [5]Meltzer EO et al. J All Clin Immun 2021 doi.org/10.1016/j.jaip.2021.07.022 [6]LifeSci Capital Report Dec 22, 2022

Haduvio Has Potential Flexibility as 1st Line or 2nd Line Therapy

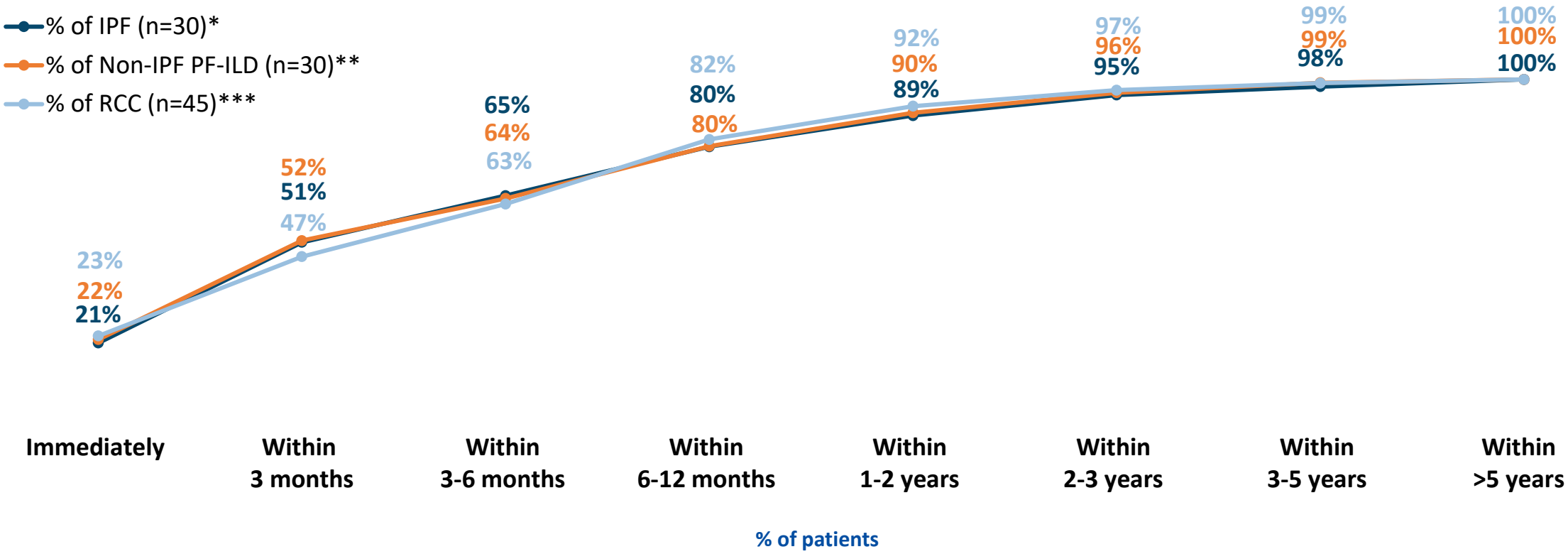
Expected placement in treatment algorithm for Haduvio



Source: Interviews and quantitative study conducted by Indegene, 2022 with US pulmonologists (n = 100) and PCPs (N=15)
Based on Target Product Profile of Haduvio
Haduvio (nalbuphine ER) is an investigational drug

Physicians Anticipate a Rapid Time to Peak for Haduvio

Avg. % of patients expected to be prescribed Haduvio



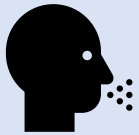
*Based on Pulmonologists who managed IPF patients with chronic cough in the last 12 months and expect to prescribe nalbuphine ER to their IPF patients

**Based on Pulmonologists who managed Non-IPF PF-ILD patients with chronic cough in the last 12 months and expect to prescribe nalbuphine ER to their PF-ILD patients

*** Trends are similar for uptake of nalbuphine ER in use for RCC patients across Pulmonologists and PCPs

Haduvio (nalbuphine ER) is an investigational drug

Haduvio Has a Large Potential Patient Opportunity by Focusing on the Most Difficult to Treat Patients with Chronic Cough

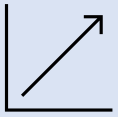


High unmet need in treating chronic cough patients with IPF, non-IPF ILDs, and RCC

Majority of chronic cough patients remain uncontrolled

Haduvio is differentiated by it's central and peripheral activity

Haduvio has the potential to be 1st or 2nd line therapy



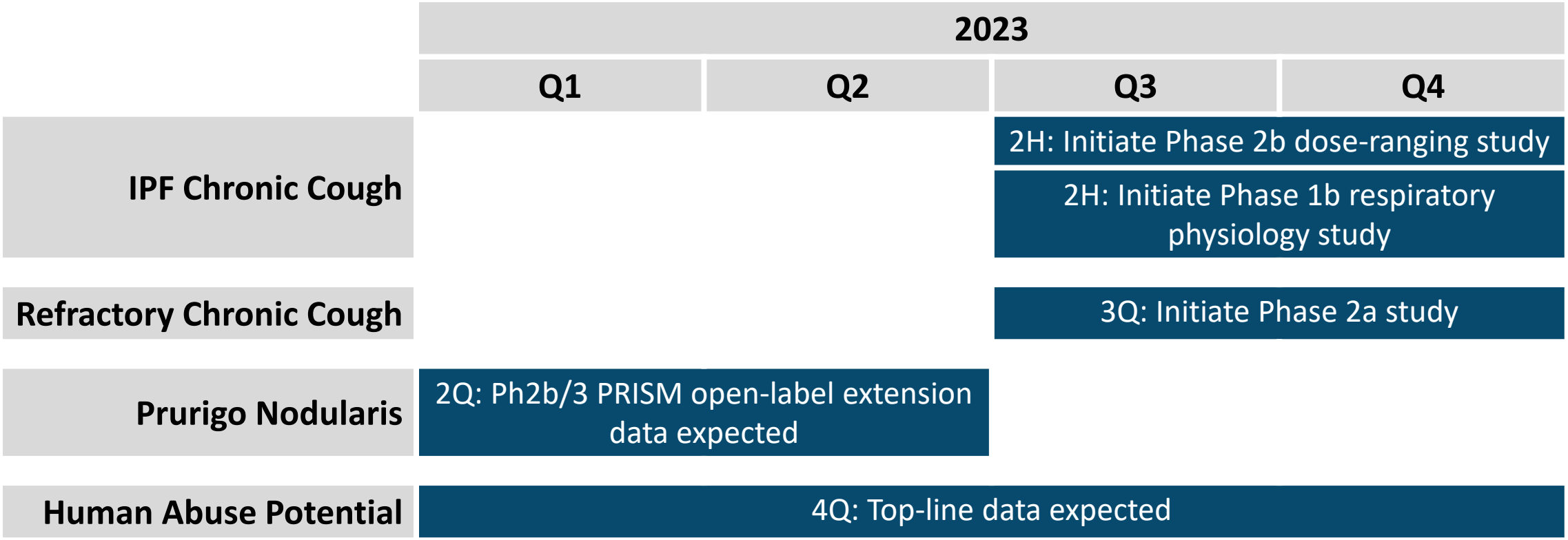
Potential for rapid adoption by pulmonologists and chronic cough patients

Closing Remarks

Jennifer Good
President and CEO

trevi™ THERAPEUTICS

Trevi 2023 Anticipated Next Steps and Financial Position



Cash and Investments

- $111.3M in cash and investments as of 3/31/2023
- Cash runway expected into 2026

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