Corporate Presentation

June 2022

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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 Significant Across Both Lead Clinical Programs

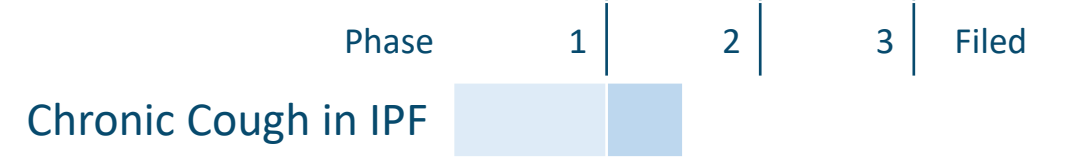
PRISM
Pruritus Relief through Itch-Scratch Modulation

Prurigo Nodularis

- Statistically significant for the primary efficacy endpoint measured by a 4-point reduction in the WI-NRS (p=0.0157).
- FDA Fast Track designation granted for moderate to severe pruritus in PN.

CANAL

Chronic Cough in Idiopathic Pulmonary Fibrosis



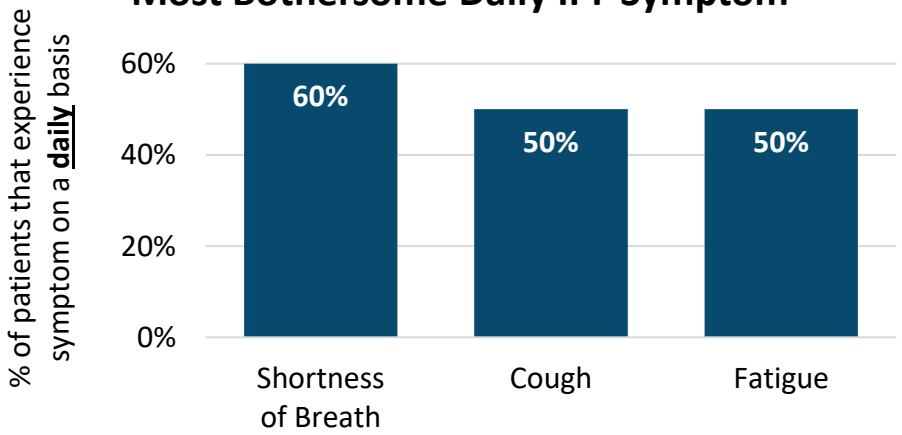
- Announced positive result from planned interim analysis (p<0.0001) in Ph2 trial. Ended enrollment and accelerating development.
- Data on full set of subjects expected in 3Q 2022.

Attractive Categories for Lead Indications

Chronic Cough in Idiopathic Pulmonary Fibrosis

- ✓ No approved therapies
- ✓ No oral option available
- ✓ High unmet need
- ✓ IPF is a life-threatening, debilitating disease[1]

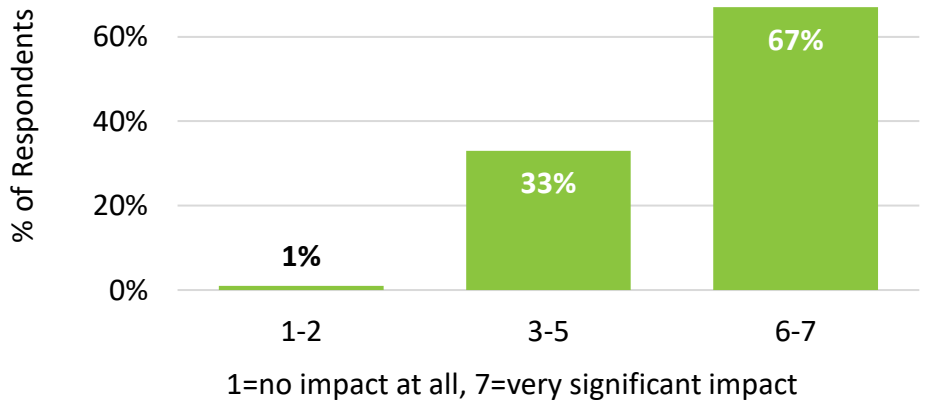
Most Bothersome Daily IPF Symptom[1]



Prurigo Nodularis

- ✓ No approved therapies
- ✓ No oral option available
- ✓ High unmet need
- ✓ PN is a serious, potentially debilitating, chronic skin condition[2,3]

Dermatologist View on PN Impact on QoL[4] (N=126)

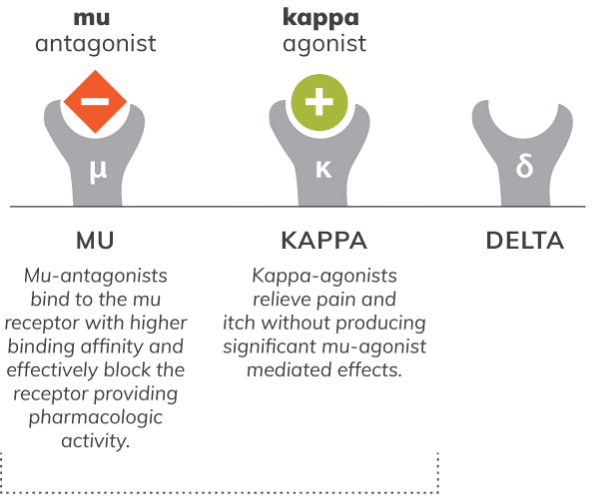


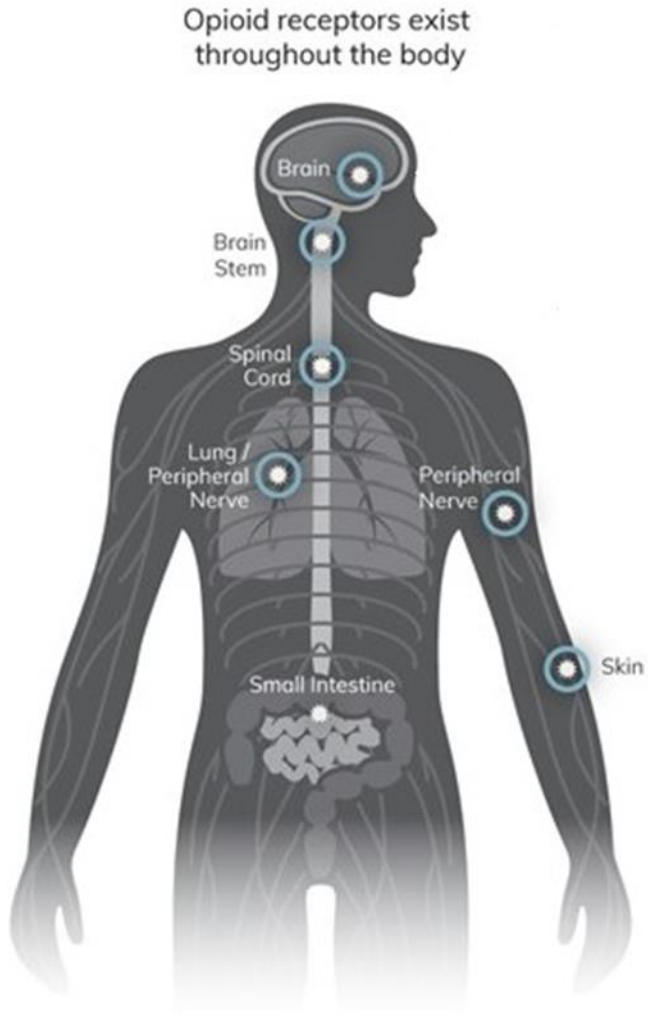
[1]Voice of the Patient – IPF Patient-focused Drug Development Initiative, 2015 [2]Iking A JEADV 2013 [3]Vaidya DC & Schwartz RA Acta Derm Croat 2008 [4]Trevi data on file

Broad Applications for Mechanism of Action of Haduvio™ (nalbuphine ER)

Haduvio™ targets the endogenous opioid system to treat serious neurologically mediated conditions

Haduvio™ has a dual mechanism of action that affects both mu and kappa opioid receptors:





Chronic Cough

- Brain stem
- Lung
- Peripheral lung nerves

Opioid receptors are believed to play an important role in the modulation of respiration and cough

Chronic Pruritus

- Reward parts of brain
- Spinal cord
- Skin
- Peripheral skin nerves

Both mu antagonists and kappa agonists have shown pharmacological activity in reducing pruritus

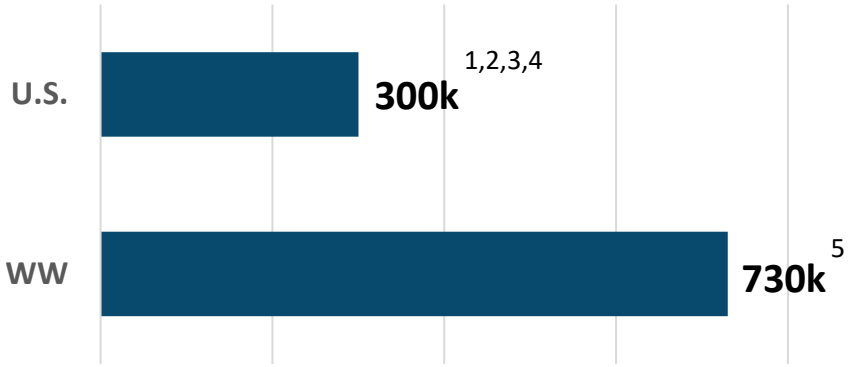
Chronic Pruritus in Prurigo Nodularis

PRISM
Pruritus Relief through Itch-Scratch Modulation

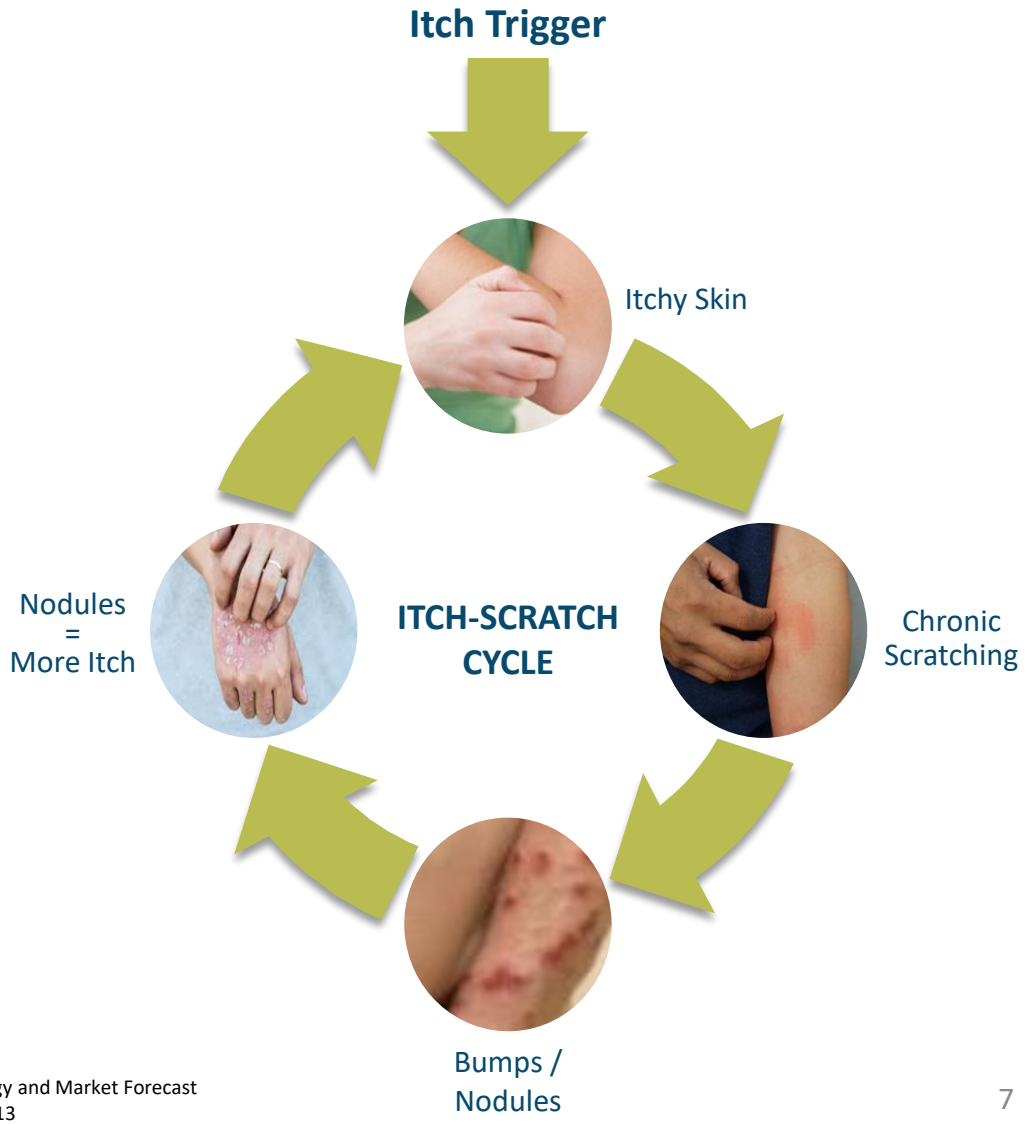
trevi THERAPEUTICS

Opportunity to be the First Oral Therapy Approved For the Treatment of Prurigo Nodularis

Current PN Prevalence



- ~40-50% of patients are uncontrolled on off-label therapies, which lack efficacy and/or have an unfavorable AE profile
- Oral therapy enables opportunity to be used in earlier lines of therapy
- Many underlying etiologies of itch, but initial scratching may create an itch-scratch cycle resulting from central and/or peripheral nervous tissue changes[6,7,8,9]



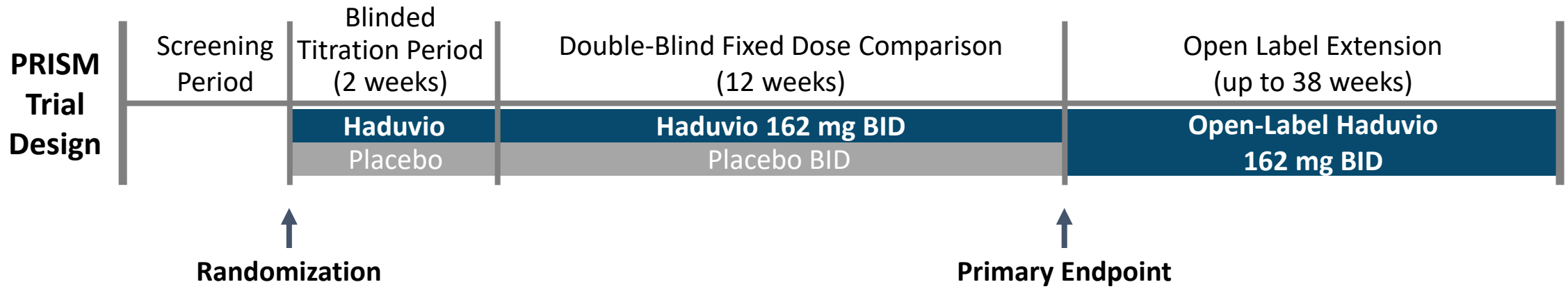
[1]Huang AH JID 2020 [2]Stander S JAAD 2020 [3]Iking A JEADV 2013 [4]Pereira M JEADV 2018 [5]Prurigo Nodularis - Market Insights, Epidemiology and Market Forecast
[6]Eigelshoven CME Derm 2009 [7]Vaidya DC & Schwartz RA Acta Derm Croat 2008 [8]Lee MR, Shumack S Aus J Derm 2005 [9]Iking A JEADV 2013
Haduvio (nalbuphine ER) is an investigational drug

Haduvio™ (nalbuphine ER) is the First and Only Oral Therapy to Demonstrate a Positive Result in Treating Prurigo Nodularis (PN)

Haduvio demonstrated an early onset of effect to reduce itch, which improved quality of life for the patient as well as the underlying skin healing

- Primary endpoint: 25% of Haduvio subjects achieved a 4-point reduction at week 14 in WI-NRS from baseline compared to 14% of placebo subjects (p=0.0157)
- Haduvio (nalbuphine ER) was significant in reducing mean WI-NRS beginning at least at week 6 vs. placebo (p=0.0056), which was sustained through to week 14 (p=0.0003)
- Haduvio subjects experienced significantly greater improvements in ItchyQoL at week 14 from baseline vs. placebo (p=0.0002) and was statistically significant across each of the three domains (symptoms, functional limitations, and emotions)
- 55% of Haduvio subjects saw at least a 1-category improvement at week 14 in the 5-point scale in their Prurigo Activity Scale (PAS) (pruriginous lesions with excoriations), vs. 38% on placebo (p=0.006)
- The safety profile remains consistent with prior studies

Phase 2b/3 PRISM Trial Design (N=353)



Primary Efficacy Endpoint (responder analysis):

- % WI-NRS Responders for NAL-ER versus PBO
- Responder = 4-point reduction from baseline at Week 14

Key Secondary Endpoints (change from baseline):

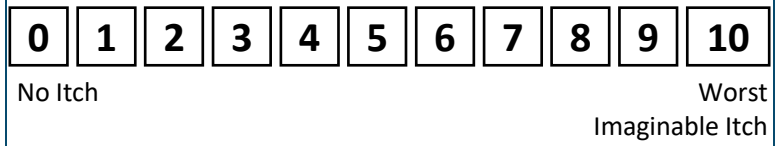
- QoL (ItchyQoL)
- Skin lesions (Prurigo Activity Score Question 5a)
- Sleep disturbances (PROMIS Sleep Disturbance Short Form 8a)

Open Label Extension:

- 99% of all subjects who reached Week 14 have continued into the open label extension
- Long-term safety
- Durability of effect
- Lesion healing

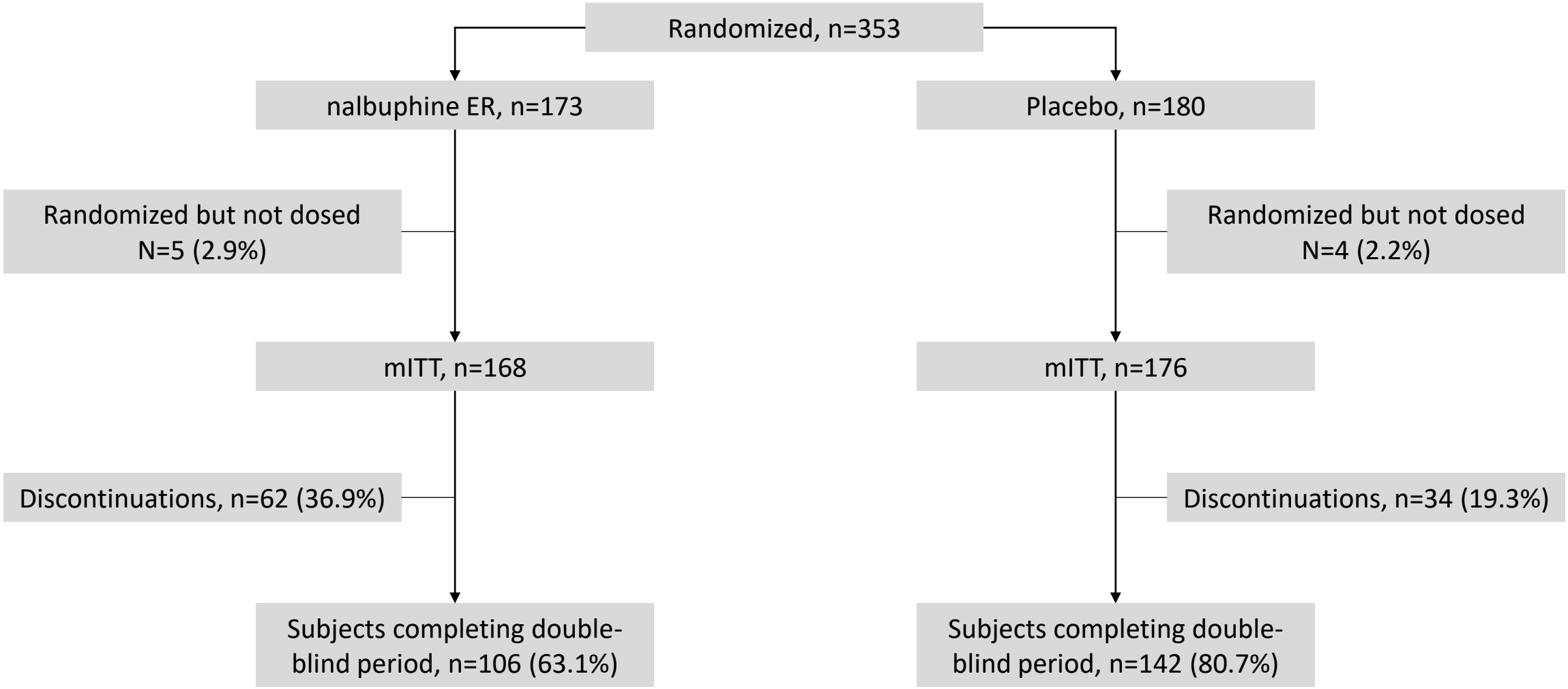
www.clinicaltrials.gov: NCT03497975
Haduvio (nalbuphine ER) is an investigational drug

Primary and Key Secondary Scales

Worst Itch NRS (WI-NRS)	ItchyQoL™	Prurigo Activity Score (PAS) Question 5a
How would you rate your most severe itching over the past 24 hours? 0 = No Itch 10 = Worst Imaginable Itch Numerical Rating Scale  	How often during the past week do these statements apply to you? 22 questions (across 3 domains: symptoms, functional limitations, and emotions) on 5-point scale: Never Rarely Sometimes Often All the Time	Please mark the respective percentage in comparison to all pruriginous lesions: a) Pruriginous lesions with excoriations/crusts: 0% 1-25% 26-50% 51-75% 76-100%

ItchyQoL ©2004, 2012 Emory University
Haduvio (nalbuphine ER) is an investigational drug

PRISM Patient Disposition



PRISM Baseline Characteristics (mITT)

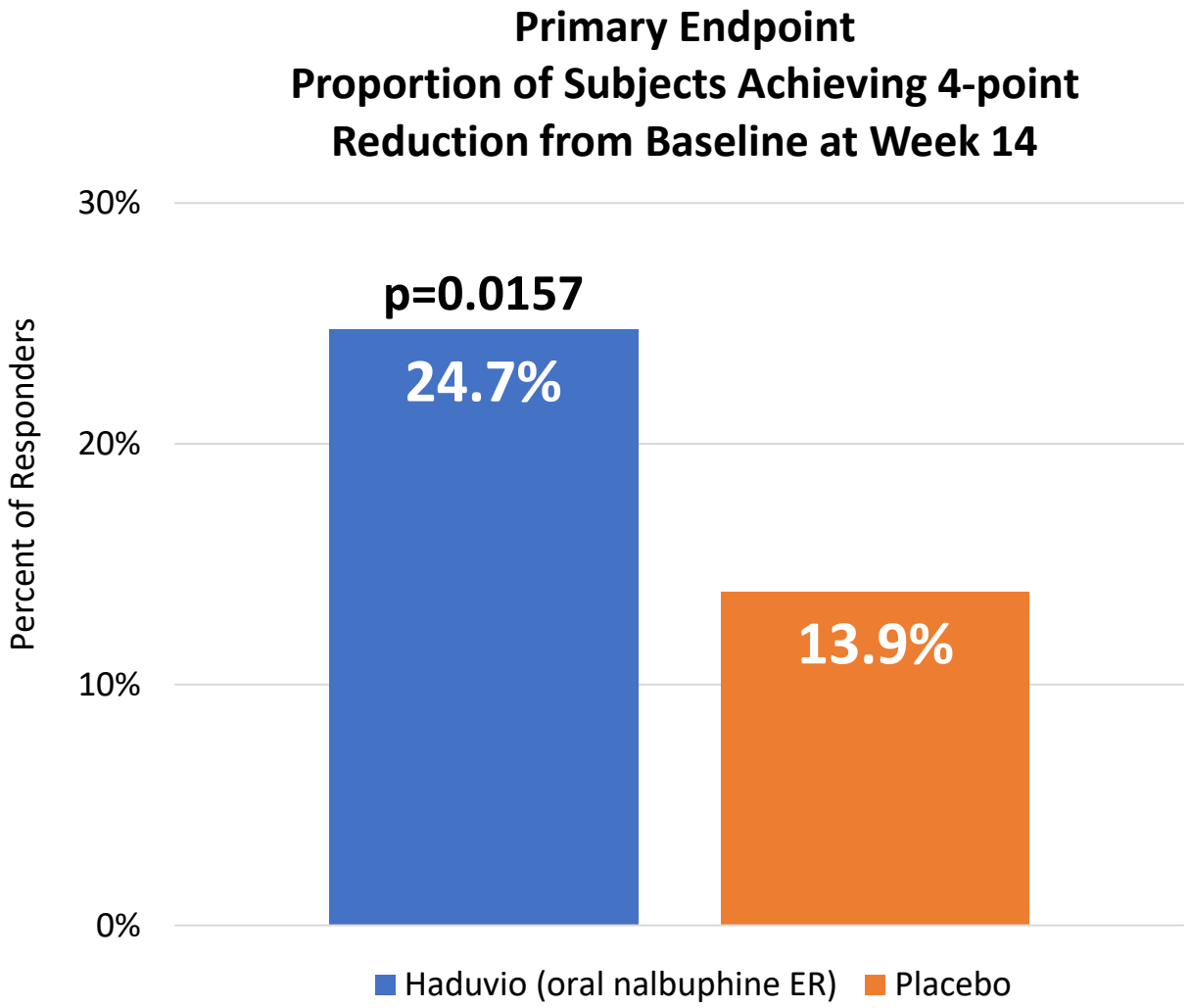
	Haduvio (oral nalbuphine ER)	Placebo	Total
Number of subjects, n	168	176	344
Baseline WI-NRS, mean	8.6	8.7	8.6
Baseline number of nodules, (%)			
1-19	10.1	12.5	11.3
20-100	60.1	52.8	56.4
>100	29.8	34.7	32.3
Age (year), mean	59.6	55.9	57.7
Sex, female (%)	59.5	63.6	61.6
Race			
Asian	6 (4%)	7 (4%)	13 (4%)
Black or African American	24 (14%)	23 (13%)	47 (14%)
Native Hawaiian/Other Pacific Islander	6 (4%)	11 (6%)	17 (5%)
White	132 (79%)	134 (76%)	266 (77%)
Multiple	-	1 (1%)	1 (0.3%)
Region			
Europe	99 (59%)	103 (59%)	202 (59%)
North America	69 (41%)	73 (42%)	142 (41%)

Haduvio Demonstrated Statistically Significant Results on the Primary Efficacy Endpoint in Prurigo Nodularis

Statistically significant reduction in primary endpoint at week 14 (p=0.0157).

Efficacy subgroup analyses corroborates primary endpoint when evaluating age (≥40 years), gender, or geography (US, EU).

Haduvio (nalbuphine ER) is the first and only oral therapy to show a positive result in treating prurigo nodularis.

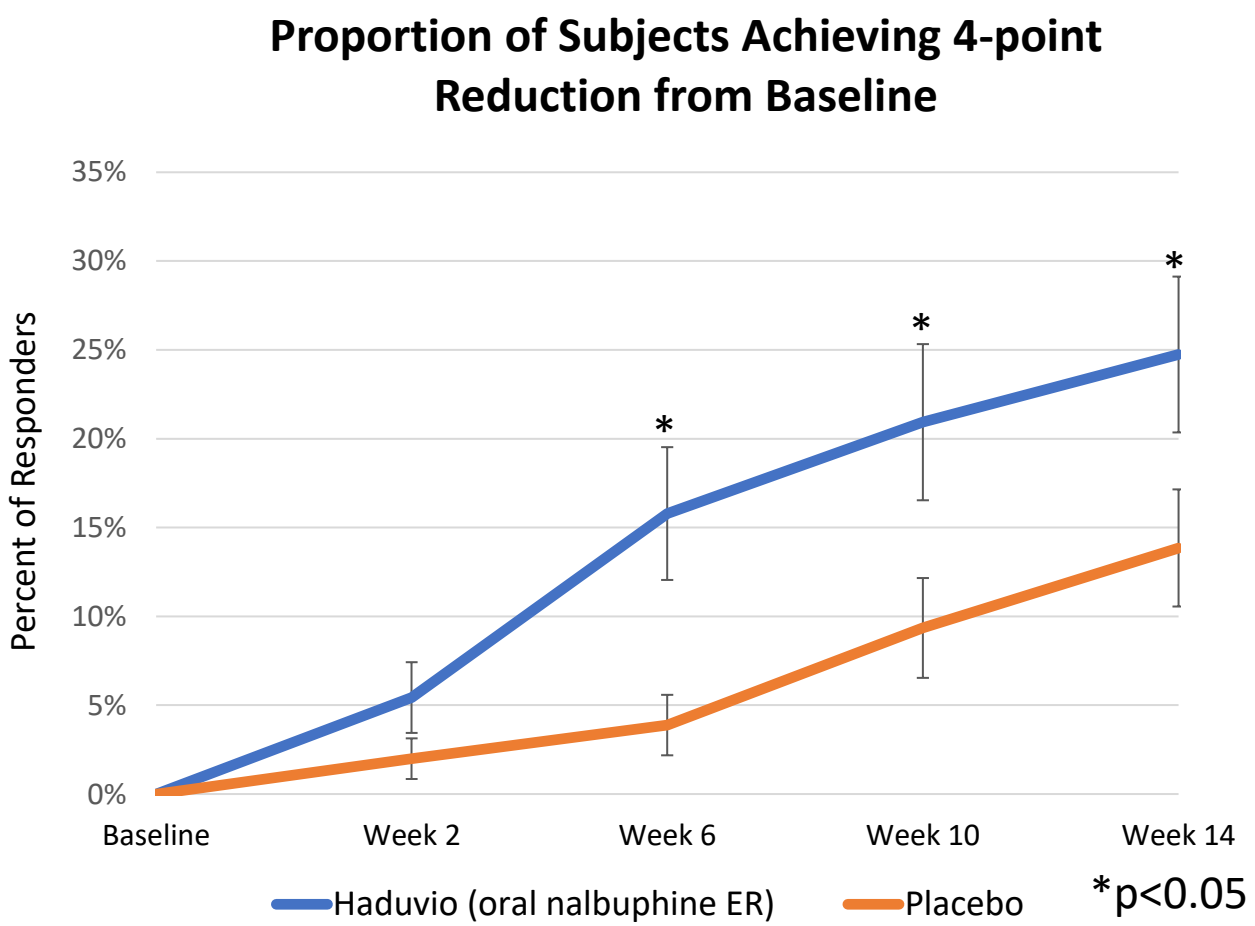


Haduvio (nalbuphine ER) is an investigational drug

Haduvio's Response Separates From Placebo as Early as Week 6 and was Sustained Over the 14-week Treatment Period

Proportion of responders with a 4-point reduction from baseline was statistically significant as early as week 6 (p=0.003)

Pruritus reduction and the percent of 4-point responders appears to continue to increase over time and we will get more data in the open label extension



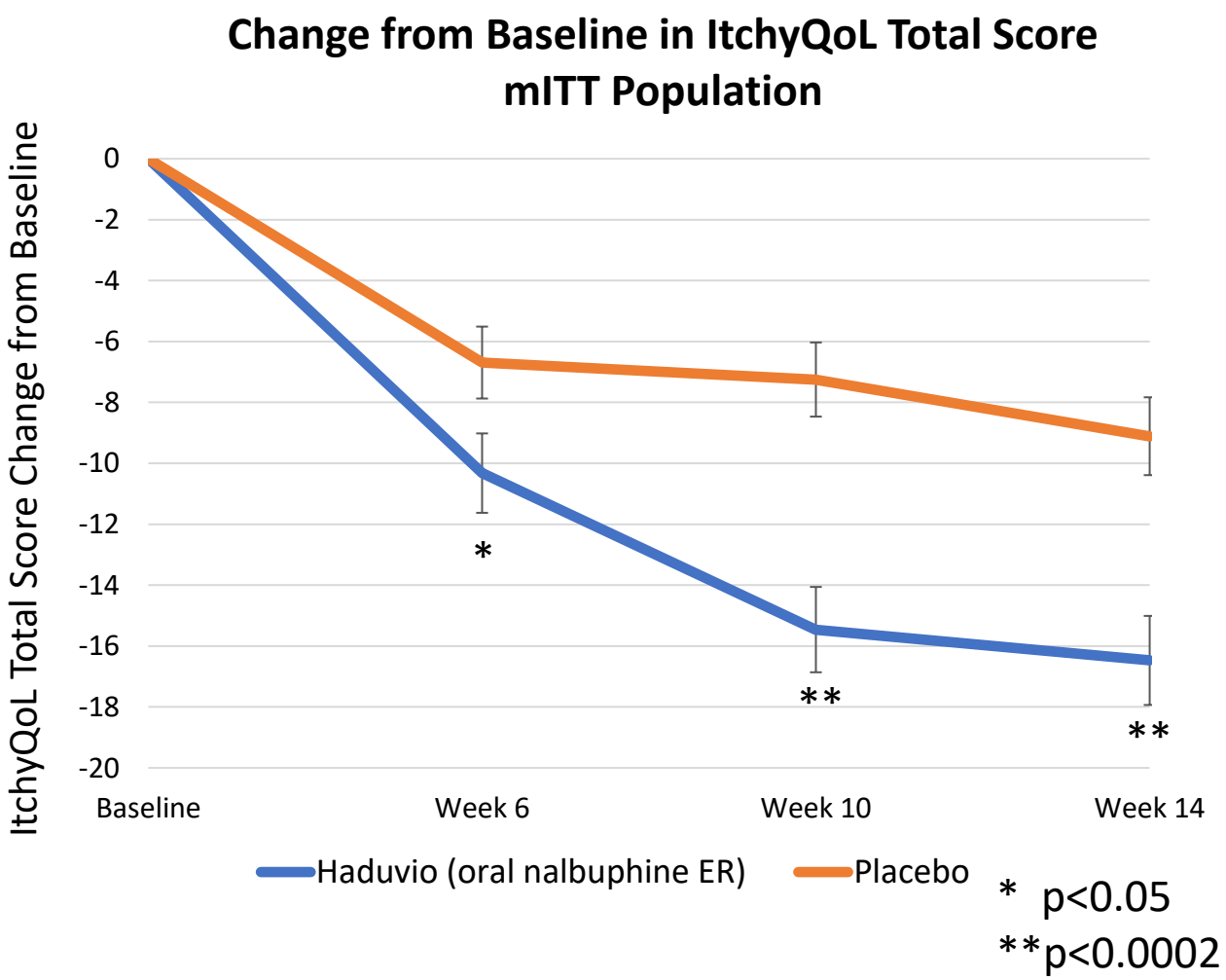
Subjects Self-Reported an Improvement in their Quality-of-Life Associated with Itch (ItchyQoL™), which was Significant Across All Domains

Haduvio subjects experienced significantly greater improvements in ItchyQoL at week 14 vs. placebo (p=0.0002)

At week 14, the ItchyQoL was statistically significant across each of the three domains (symptoms, functional limitations, and emotions).

The ItchyQoL consists of 22 pruritus-specific items measuring how pruritus affects subjects' QoL in the area of symptoms related to the itch condition (6 questions), functional limitations (7 questions), and emotions (9 questions).

The subject scores each question never = 1, rarely = 2, sometimes = 3, often = 4, all the time = 5.

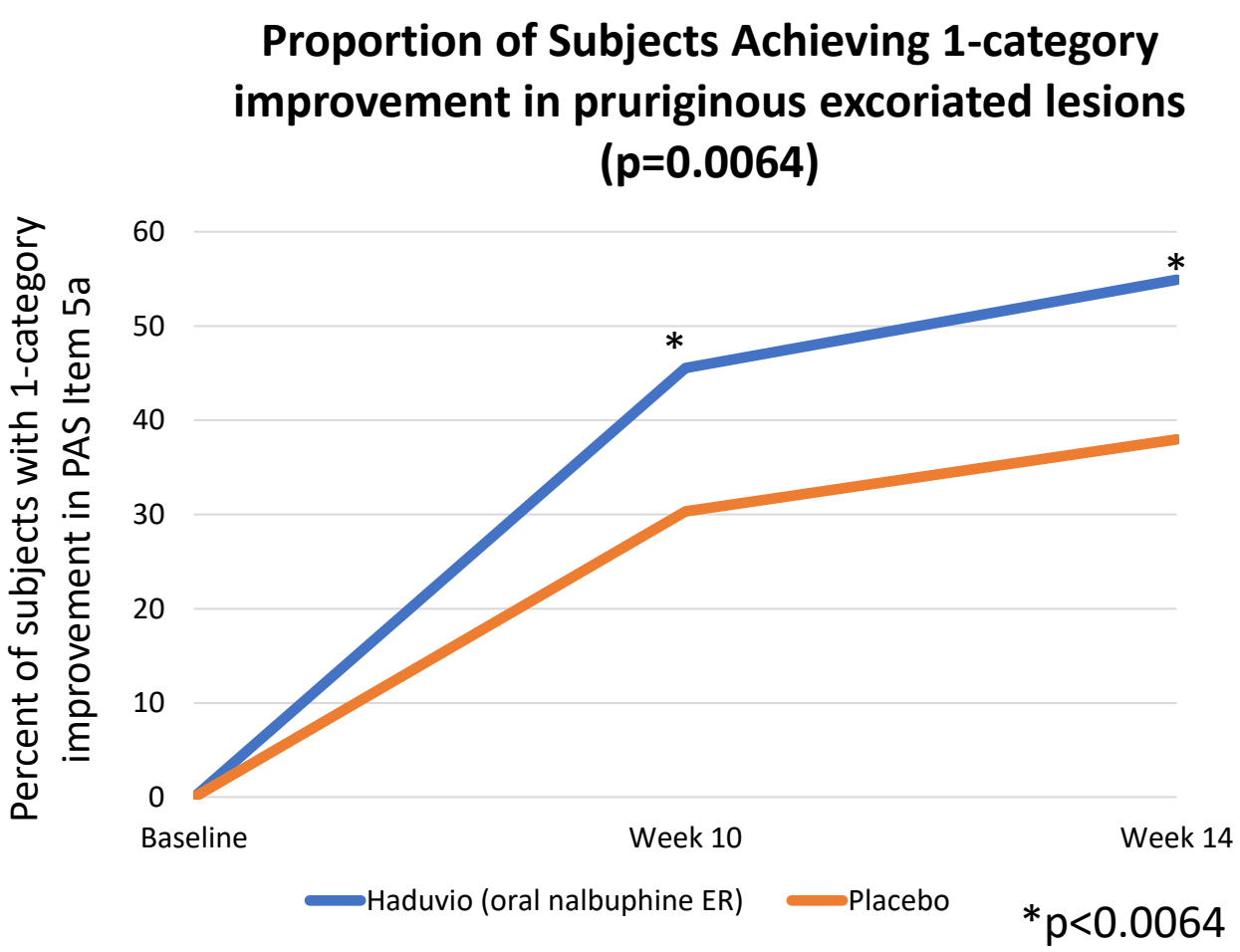


Haduvio Significantly Reduced Lesions with Excoriations

Haduvio improved lesions with excoriations as early as week 10 (p=0.002) and was sustained through week 14 (p=0.0064), which is a measurement of overall disease modification

Prurigo Activity Score (PAS) was measured at week 10 and week 14

In the open label extension, we are measuring the reduction in the number of nodules and papules to monitor disease improvement



Haduvio (nalbuphine ER) is an investigational drug

Efficacy Results Seen Throughout the Trial in Haduvio Patients

Subject A

Baseline

Week 14

Week 52

Subject B

Baseline

Week 14

Week 52

Actual Haduvio patients. Individual results may vary. Source: Data on file, Trevi Therapeutics, Inc.
Haduvio (nalbuphine ER) is an investigational drug

Summary of Treatment-Emergent Adverse Events in the Safety Population

	Haduvio 162 mg BID (N=168) n (%)	Placebo (N=176) n (%)	Total (N=344) n (%)
Subjects With any TEAE:			
- 2-week titration period	111 (66.1)	55 (31.3)	166 (48.3)
- 12-week fixed dose period	81 (48.2)	79 (44.9)	160 (46.5)
Subjects With any SAEs	8 (4.8)	6 (3.4)	14 (4.1)
	None considered to be treatment related		
Subjects With any TEAE Leading to Study Drug Discontinuation:	56 (33.3)	12 (6.8)	68 (19.7)
- 2-week titration period	33 (19.6)	5 (2.8)	38 (11.0)
- 12-week fixed dose period	23 (13.7)	7 (4.0)	30 (8.7)
Subjects With any TEAE Leading to Death	0	0	0

Abbreviations: SAE=Serious Adverse Event; TEAE=Treatment Emergent Adverse Event.
N=Number of treated subjects; n (%)=Number (%) of subjects with the event term by category.
Note: Percentages are based on the header N as the denominator in each treatment group.
Double-blind fixed dose period TEAEs are defined as AEs that either start or worsen in severity on or after the first dose of study drug in the double-blind fixed dose period (i.e. week 3 to week 14) and prior to the first dose in the extension titration period.
A Related TEAE is one whose relationship to study drug is assessed by the Investigator as definitely, probably or possibly related.
Haduvio (nalbuphine ER) is an investigational drug

Most Commonly Reported Treatment Emergent Adverse Events

Treatment-Emergent Adverse Events at ≥10% Frequency	Haduvio 162 mg BID (N=168) n (%)	Placebo N=176 n (%)	Total N=344 n (%)
Nausea	51 (30.4)	16 (9.1)	67 (19.5)
Dizziness	51 (30.4)	5 (2.8)	56 (16.3)
Headache	26 (15.5)	14 (8.0)	40 (11.6)
Constipation	26 (15.5)	7 (4.0)	33 (9.6)
Somnolence	25 (14.9)	6 (3.4)	31 (9.0)
Fatigue	23 (13.7)	10 (5.7)	33 (9.6)
Vomiting	19 (11.3)	7 (4.0)	26 (7.6)

Chronic Cough in Idiopathic Pulmonary Fibrosis (IPF)

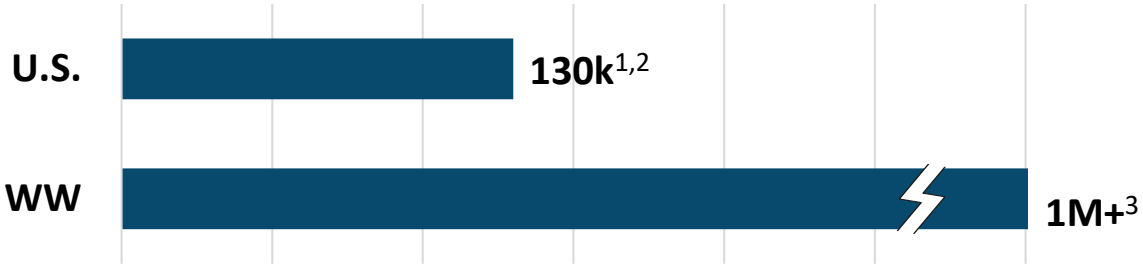
Nalbuphine ER Demonstrated Highly Statistically Significant Reduction of Chronic Cough In Idiopathic Pulmonary Fibrosis (IPF) From Ph2 Interim Analysis

Nalbuphine ER demonstrated a highly significant and consistent reduction in chronic cough associated with IPF in an interim analysis

- 77% reduction in daytime cough frequency from study baseline for nalbuphine ER in daytime cough frequency to day 22 of treatment, demonstrating a 52% placebo-adjusted reduction in the geometric mean percent change ($p<0.0001$)
- Magnitude of response is consistent across various data analyses
- Strong, consistent and supportive secondary endpoints and patient reported outcomes
- Safety profile remains consistent with prior nalbuphine ER studies in other patient populations with no new safety signal

Opportunity to be First in Class for Chronic Cough in Idiopathic Pulmonary Fibrosis

Current IPF Prevalence

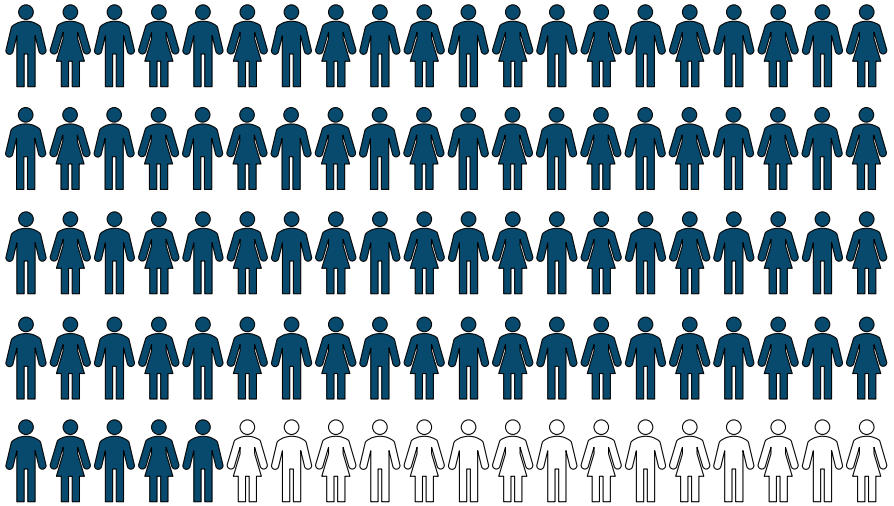


There are no approved therapies for IPF chronic cough

Current IPF therapies (anti-fibrotics), which have not been shown to reverse disease progression, are not labeled to reduce cough frequency/severity

~85%

of IPF patients suffer from chronic cough[4]



[1]Raghu G et al. Eur Resp J 2016 [2]Raghu G et al. Am J Resp Care Med 2006 [3]Nalsnyk L et al. Eur Resp Rev 2012 [4]Ryerson CJ et al. Respirology 2011

The Significant Role of Chronic Cough in IPF

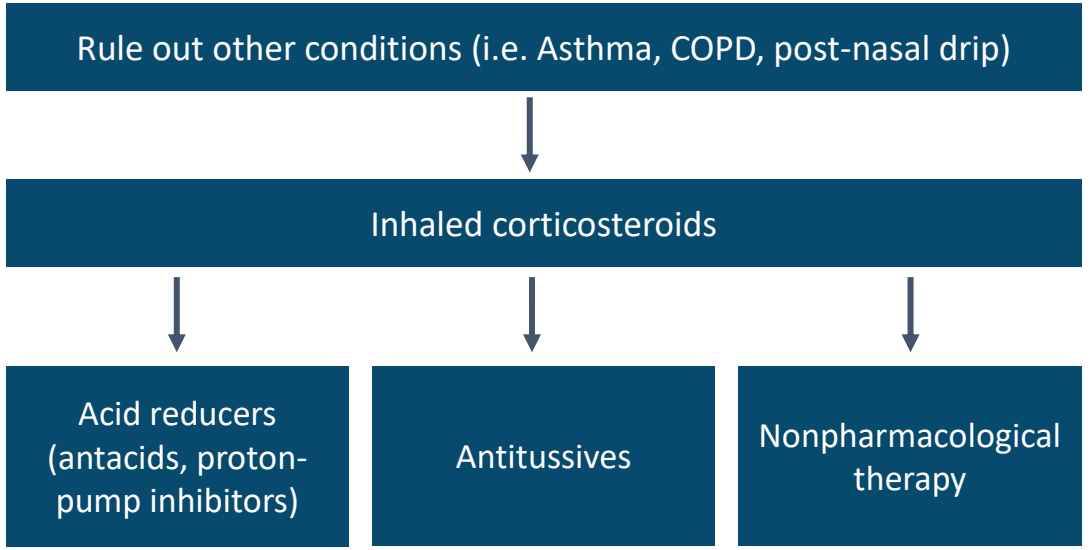
- **IPF is a high burden disease** that has a high impact on QoL, e.g.:[1-5]
  - Coughing can increase feelings of anxiety as it induces breathlessness
  - Coughing spells or episodes lead to significant fatigue, air hunger, peripheral oxygen desaturation
  - Patients may also experience cough-related urinary incontinence
  - 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
- While the pathophysiology of chronic cough in IPF is not fully understood, it is believed to be a multifactorial causation, including mechanical, chemical, and biological factors.[6]
- Chronic cough may also **contribute to enhanced activation of profibrotic** mechanisms and **disease worsening in IPF** [7]
- 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]

226-520

Median coughs per day of an IPF patient.[5,9]
The urge to cough cannot be relieved by coughing.[4]

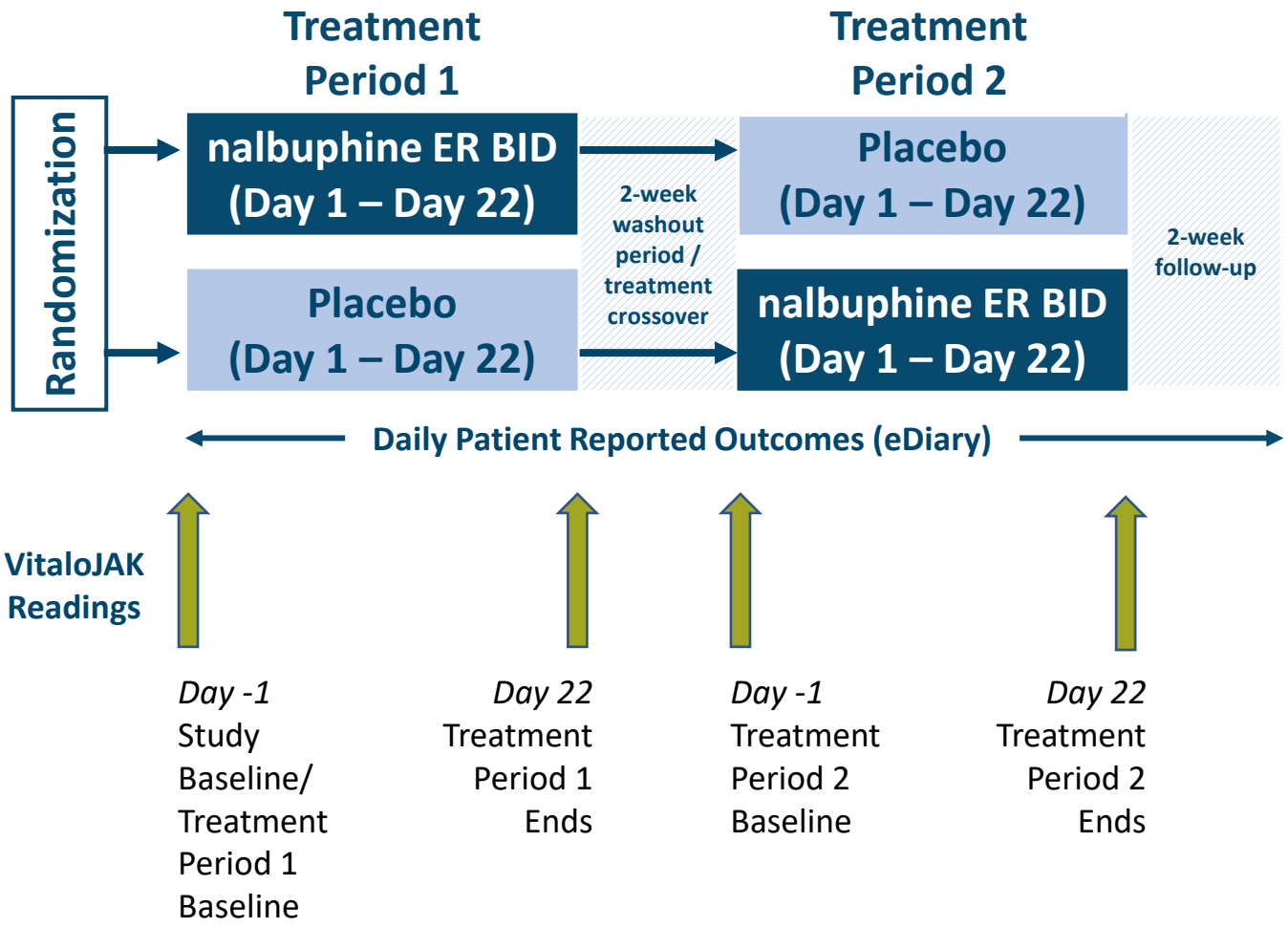
Treatment pathway (simplified)[10]

No currently approved treatment options



[1]vanManen M et al. *Ther Adv Respir Dis* 2017 doi: 10.1177/1753465816686743 [2]Wakwaya Y et al. *Chest* 2021 DOI: 10.1016/j.chest.2021.05.071 [3]Bradia F et al. *Rev Mal Respir* 2009 DOI: 10.1016/s0761-8425(09)74668-6 [4]Swigris JJ et al. Health Qual Life Outcomes 2005 DOI: 10.1186/1477-7525-3-61 [5]Key AL et al. Cough 2010 DOI: 10.1186/1745-9974-6-4 [6]Mann J et al. *Front. Rehabilit. Sci.* 2021. doi.org/10.3389/fresc.2021.751798 [7]VanManen M et al. ERS 2016 DOI: 10.1183/16000617.0090-2015 [8]Ryerson CJ et al. *Resp* 2011 DOI: 10.1111/j.1440-1843.2011.01996.x [9]VanManen M et al. Am J Respir Crit Care Med 2015; 191: A4422 [10]Morice AH et al. Eur Respir J 2020 DOI: 10.1183/13993003.01136-2019

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



PRIMARY ENDPOINT

Geometric mean percent change in daytime cough frequency from study baseline as measured by a digital cough monitor (VitaloJAK®, a validated 510k cleared device) between the nalbuphine ER and placebo treatments

SECONDARY ENDPOINTS

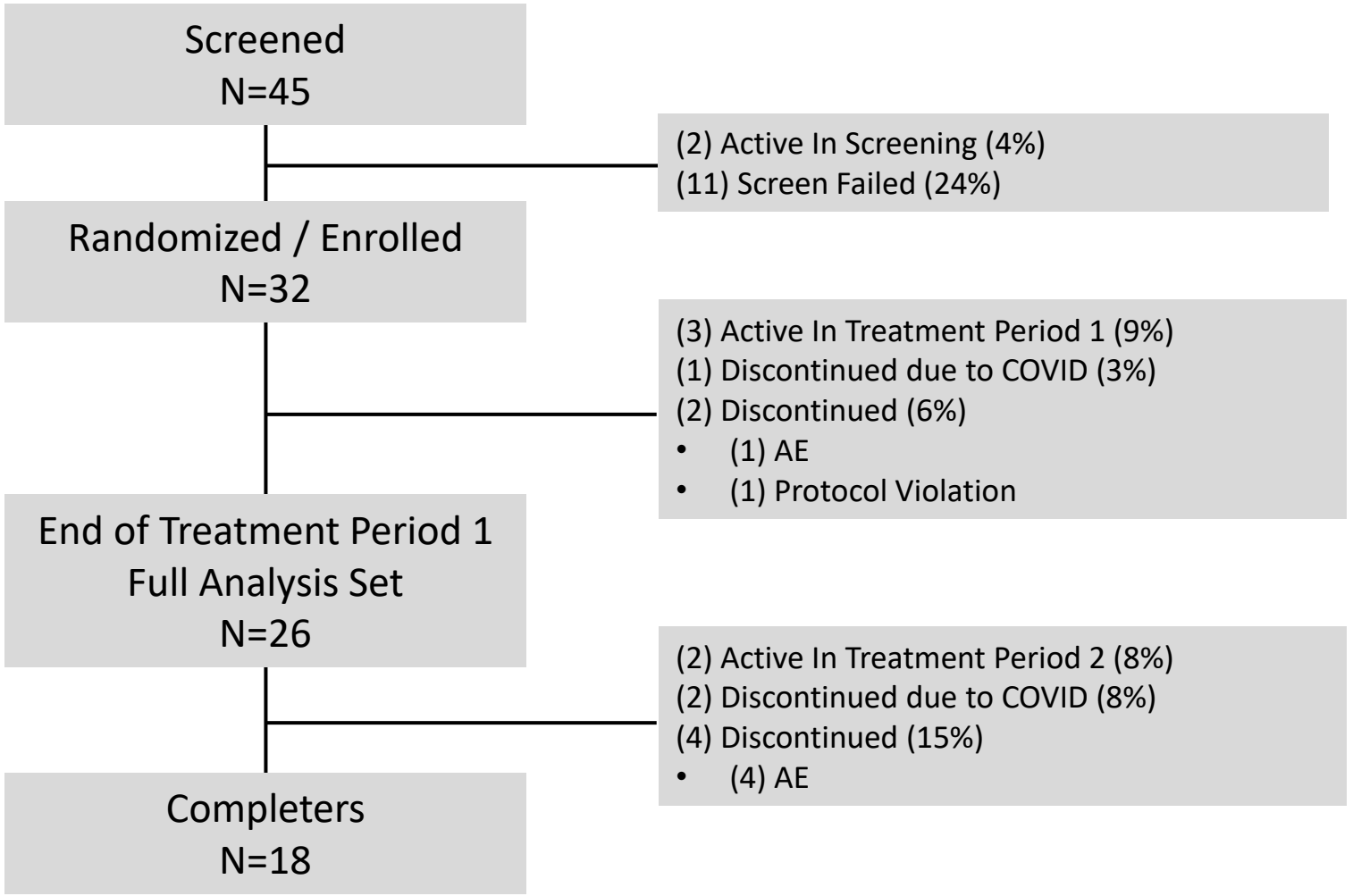
Cough severity
Fatigue
Dyspnea

NALBUPHINE ER

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

www.clinicaltrials.gov: NCT04030026
nalbuphine ER is an investigational drug

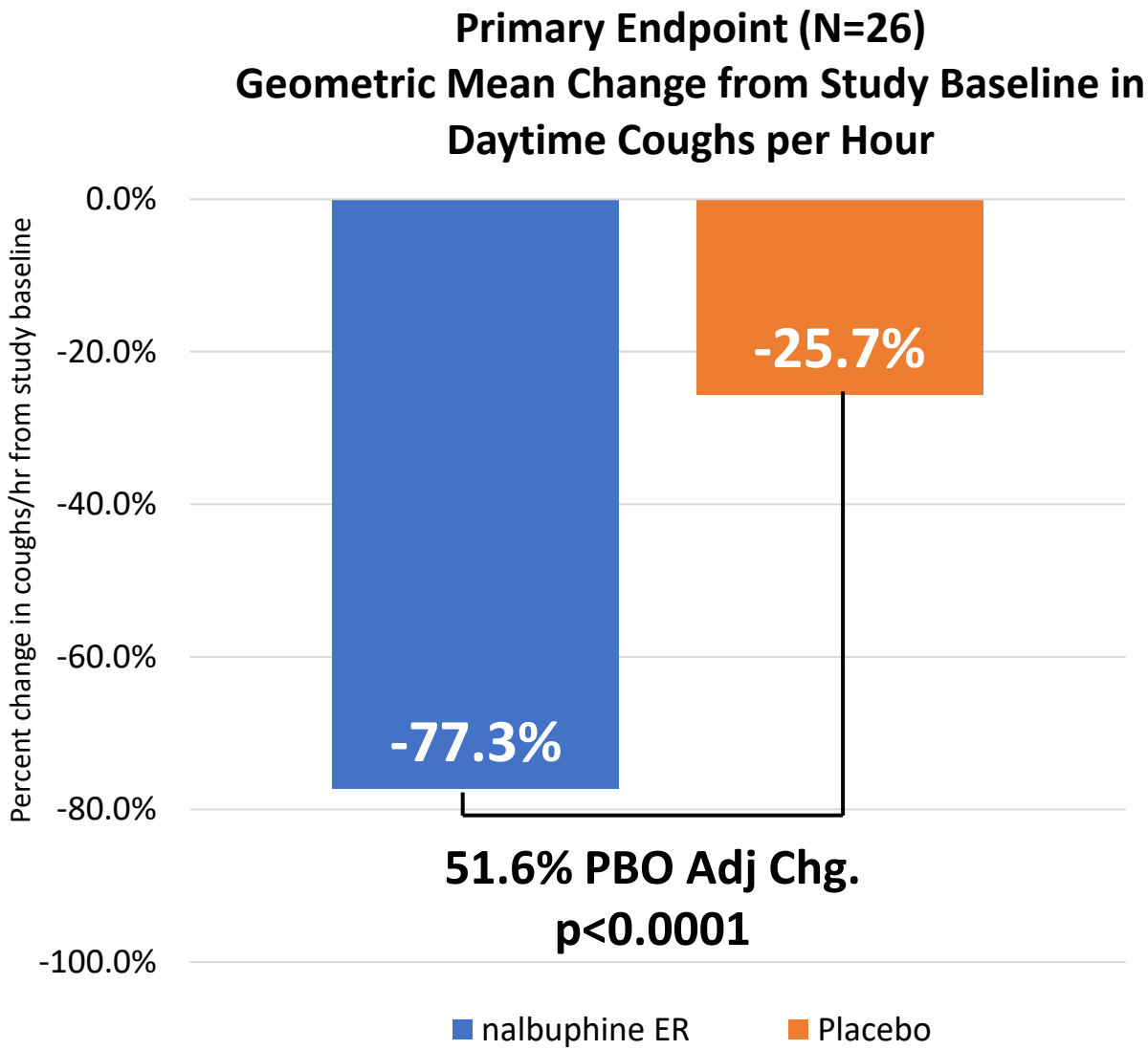
CANAL Interim Analysis Subject Disposition
Data Cut-off: 28 JAN 2022



CANAL Trial Interim Analysis Baseline Characteristics

	Full Analysis Set	Completers (Subjects Completing Both Treatment Periods)
Number of subjects, n	26	18
Male, n (%)	22 (84.6%)	14 (77.8%)
Age (years), mean	72	71
On Anti-Fibrotic, n (%)	10 (38%)	6 (33%)
Daytime cough frequency (coughs/hour): Mean	31	31
Median	20.6	22.4
Min-Max	3.18 - 92.35	3.18 - 77.18

Primary Efficacy Endpoint Achieved Statistically Significant Reduction in Cough Frequency with nalbuphine ER

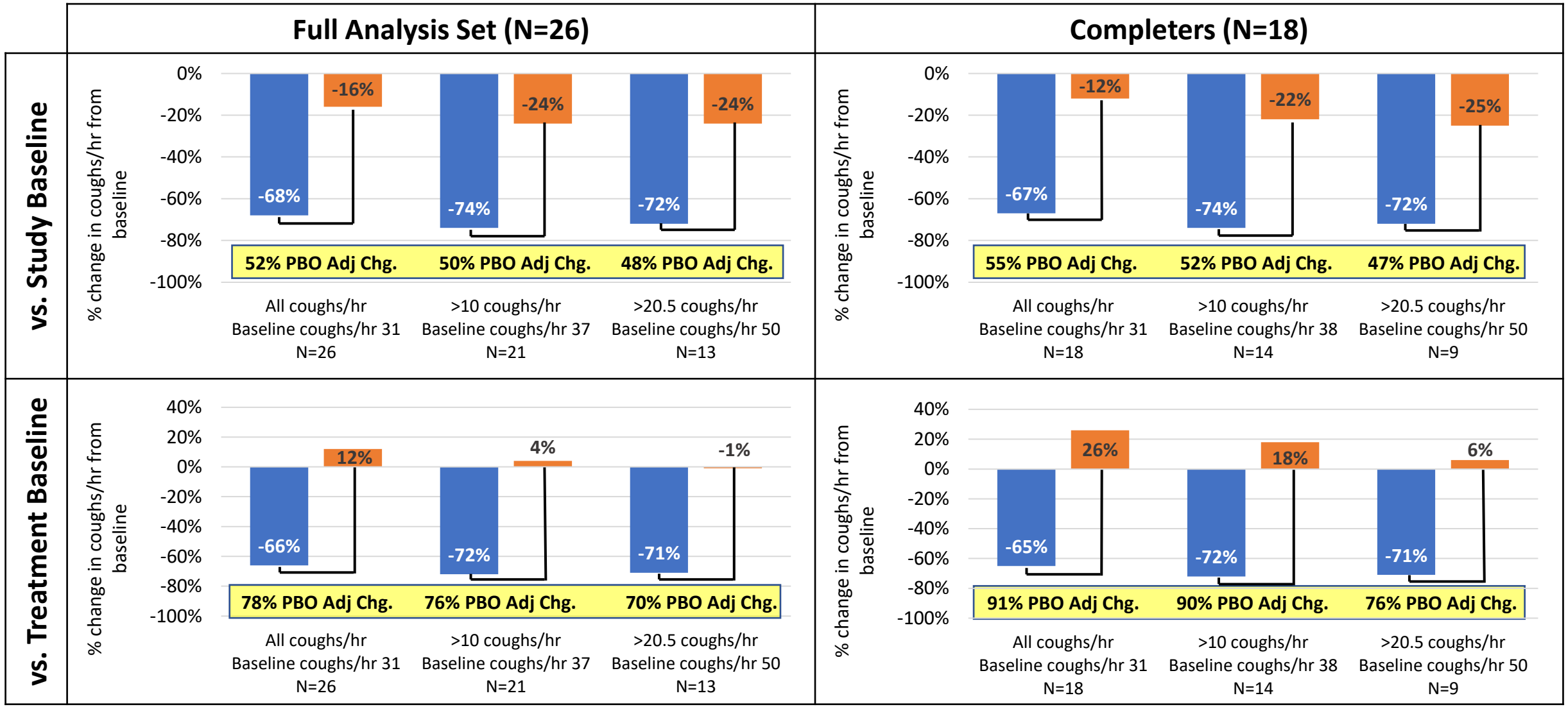


The VitaloJAK® Cough Monitor provides a fully validated system for objective measurement of cough.

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

Primary Endpoint calculated as geometric mean percent change in daytime cough frequency from study baseline
nalbuphine ER is an investigational drug

Magnitude of nalbuphine ER Effect Remains Consistent Across Various Analyses



Endpoint calculated as arithmetic mean percent change in daytime cough frequency from study baseline
nalbuphine ER is an investigational drug

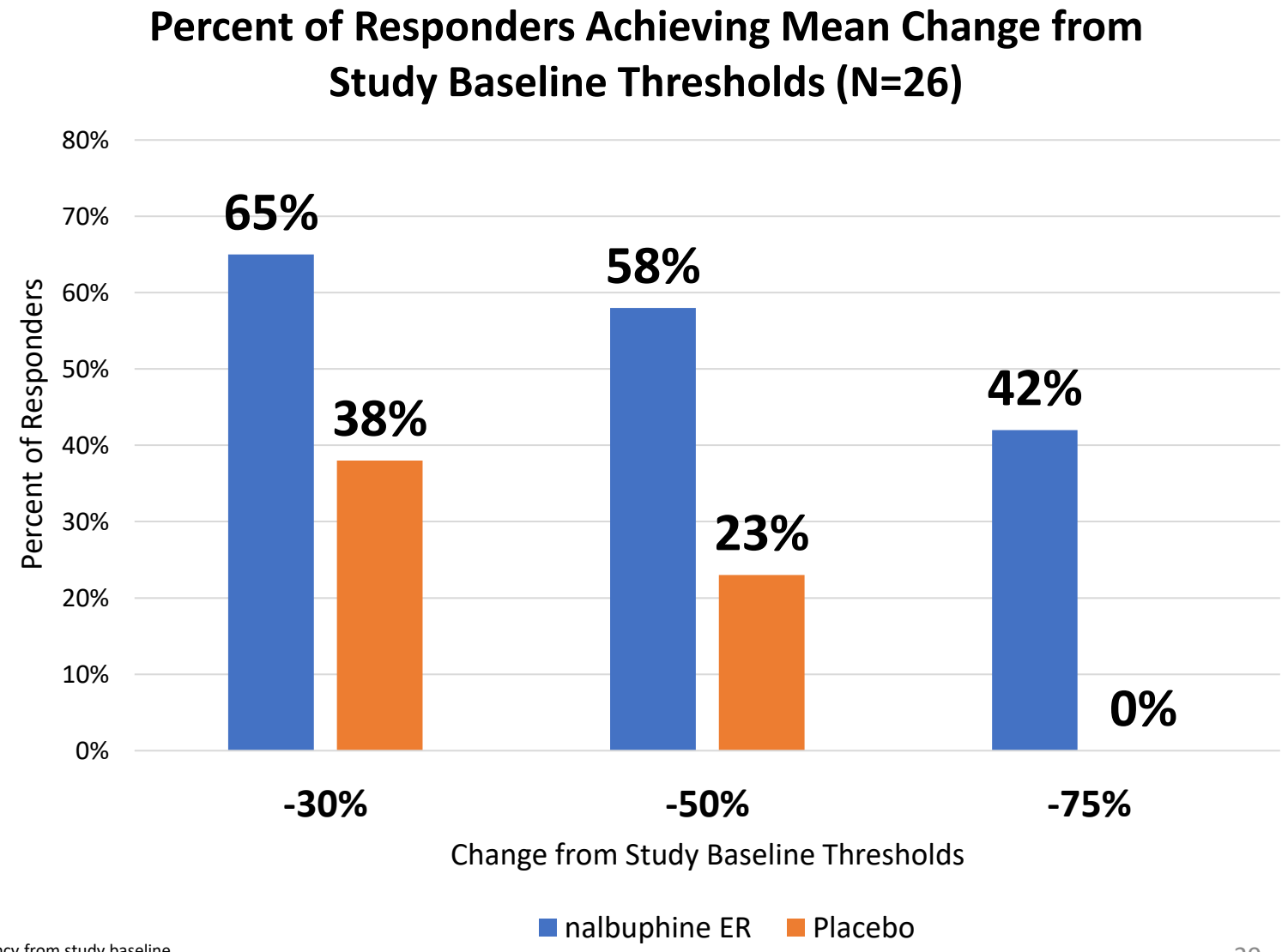
nalbuphine ER Placebo

Responder Analyses
Clear Separation Between nalbuphine ER vs. Placebo at All Levels

Assessed the magnitude of response by defining the percentage of reduction achieved by treatment response categories ranging from 30% to 75% improvement

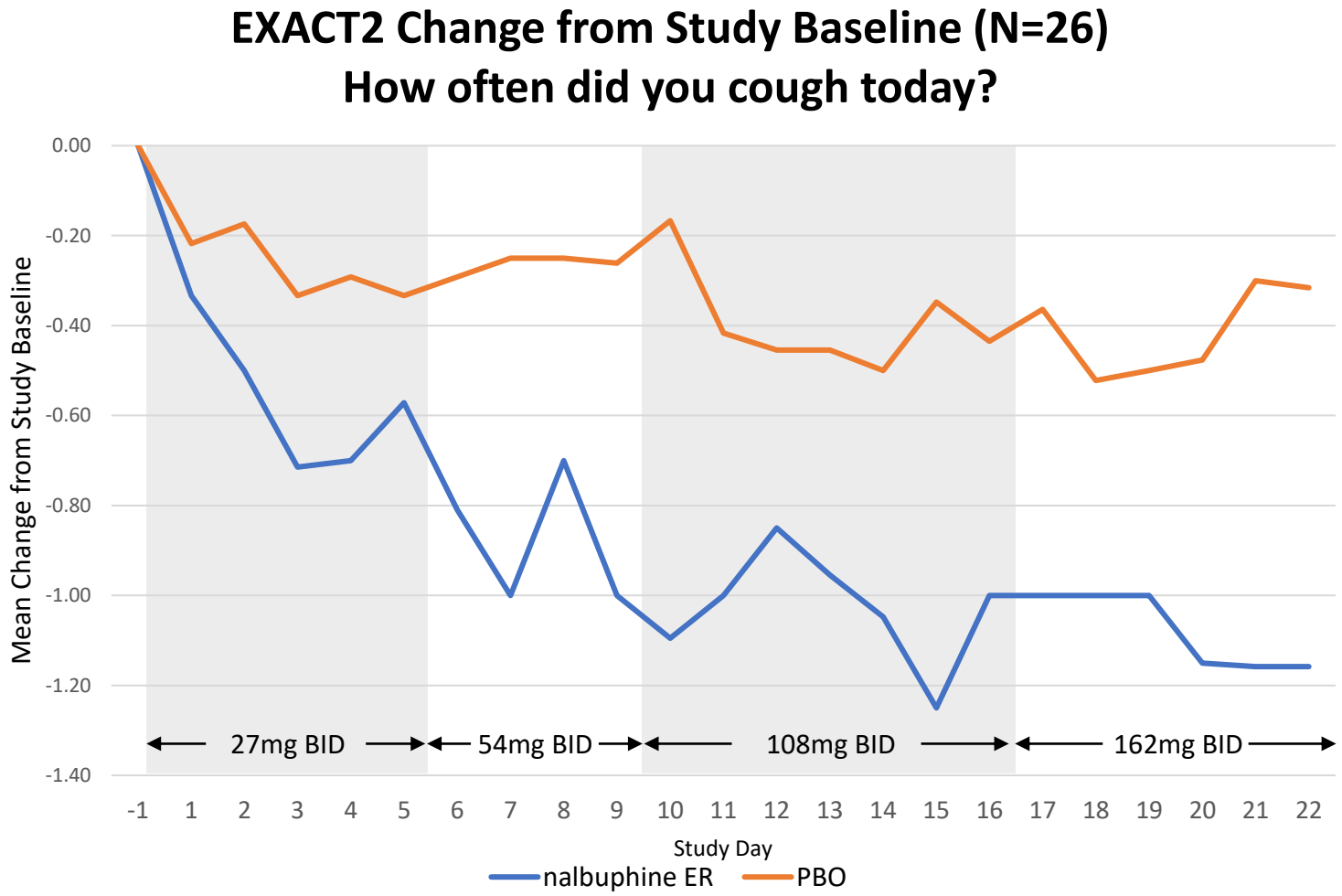
Nalbuphine ER outperforms placebo in each analysis

42% of nalbuphine ER treated subjects obtained a 75% reduction in their cough counts compared to 0% of placebo treated subjects



Endpoint calculated as arithmetic mean percent change in daytime cough frequency from study baseline
nalbuphine ER is an investigational drug

Preliminary EXACT2 Analysis Shows Early Separation and is Consistent with the Objective Cough Monitor at the End of the Treatment Period



Endpoint calculated as arithmetic mean change from study baseline
nalbuphine ER is an investigational drug

Nalbuphine ER Safety Summary

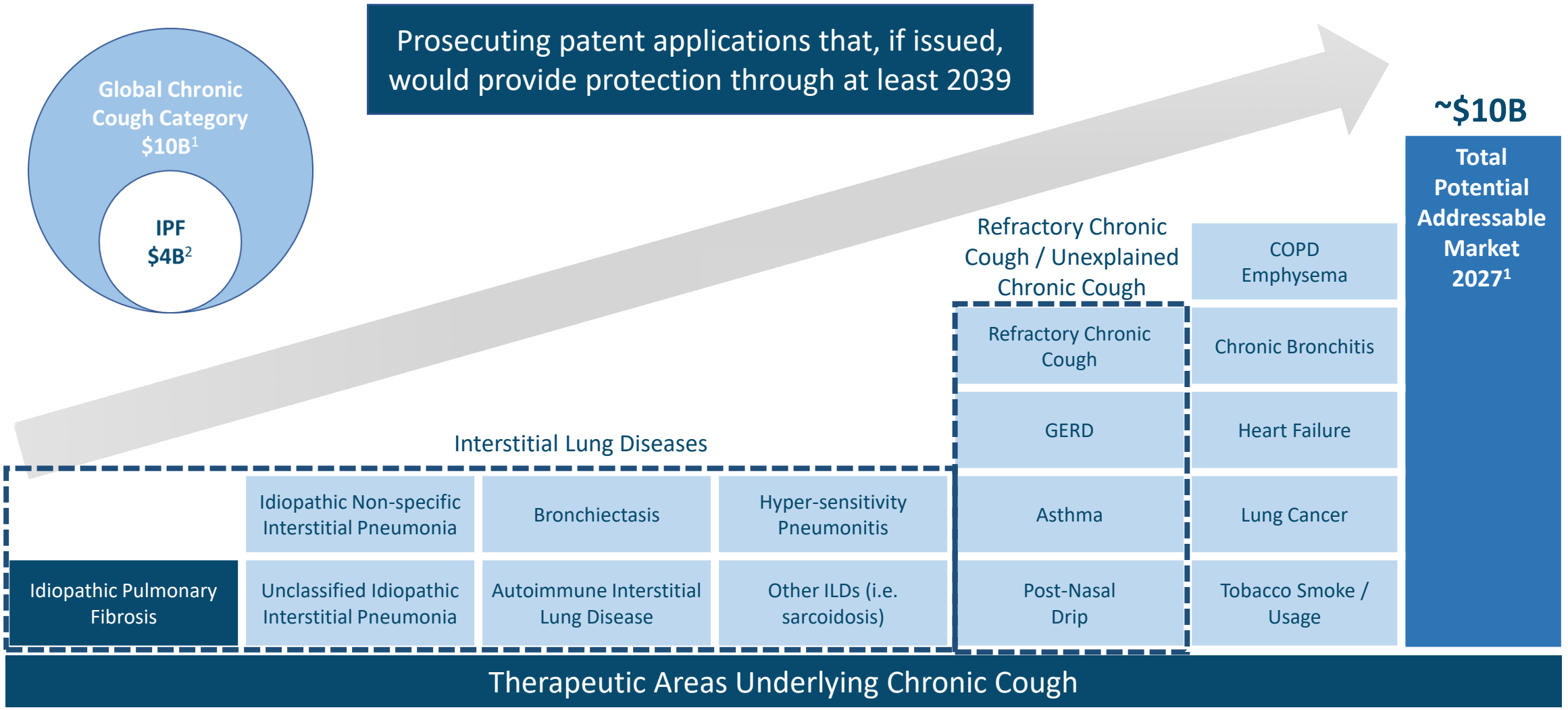
No new safety-related issues have arisen in the study and the adverse event profile of the drug in the IPF subject population is consistent with the safety profile noted in all other past studies where nalbuphine ER has been investigated in a variety of medical conditions

Nalbuphine ER has been dosed in > 1,000 subjects

<u>CANAL Safety:</u>

- DSMB continues to oversee safety in keeping with DSMB Charter
  - No safety concerns have been raised by the DSMB overseeing the conduct of the study
- No reported deaths and 1 reported Serious Adverse Event (i.e., pneumonia) not considered treatment related
- 5 AEs have resulted in discontinuation (16%):
  - 1 anorexia, 1 depression, 1 nausea/vomiting, 1 insomnia/fatigue, 1 agitation/anxiety/dyspnea

Potential Market Opportunity Across a Broad Array of Chronic Cough Conditions



[1]2027 est. The Insight Partners Jun 2020 [2]2028 est. VPA Research Idiopathic Pulmonary Fibrosis Report Feb 2021

Strong Financial Foundation to Advance Pipeline

- **Strong Cash Position**
  - ~$78M in pro-forma cash position as of June 30, 2022
    - $55M PIPE executed at market with Frazier, Venrock, Fairmount and NEA (existing investor)

- **Term loan with SVB - $12.2M outstanding as of 5/1/22**
  - Will be paid off Q1 2024

- **Cash runway into Q1 2024**

Near Term News Flow and Next Steps

IPF Cough Program:

CANAL

- 3Q 2022: CANAL trial topline data from full set of subjects
- 3Q 2022: FDA Meeting to discuss Ph2b/3 study of cough in IPF patients
- 1H 2023: Expect to initiate Ph2b/3 study of cough in IPF patients

PN Program:

PRISM
Pruritus Relief through Itch-Scratch Modulation

- 2H 2022: PRISM open-label extension completed
- 2H 2022: Develop strategy for next study, request EoPh2 meeting with FDA, and prepare to initiate second pivotal PN trial

trevi THERAPEUTICS