Corporate Presentation

May 2022

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 the expected timing of reporting top-line data from both Trevi's Phase 2b/3 PRISM trial of Haduvio in subjects with PN and Phase 2 CANAL trial of Haduvio in IPF subjects with chronic cough; Trevi's business plans and objectives, including future plans or expectations for Trevi's product candidates; 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, including with respect to the timing of reporting top-line data from both Trevi's Phase 2b/3 PRISM trial and Phase 2 CANAL trial; uncertainties regarding Trevi's ability to execute on its strategy; the risk that positive interim or top-line results from a clinical trial may not necessarily be predictive of the results of the completed trial or other future or ongoing clinical trials; potential regulatory developments in the United States and foreign countries; uncertainties regarding fast track designation and the effect such status could have on the regulatory review or approval process; uncertainties inherent in estimating Trevi's cash runway, future expenses and other financial results, including Trevi's ability to continue as a going concern, comply with its obligations under its loan facility and fund future operations; 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; uncertainties regarding Trevi's ability to maintain its listing on the Nasdaq Global Market; as well as other risks and uncertainties set forth in the annual report on Form 10-K for the quarter and year ended December 31, 2021 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.

HADUVIO™ (nalbuphine ER) Advancing Two Lead Clinical Programs

CANAL

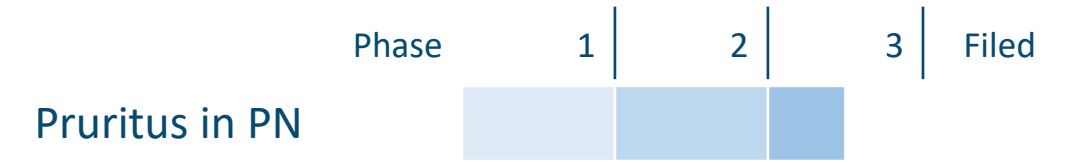
Chronic Cough in Idiopathic Pulmonary Fibrosis

- Phase 2 proof-of-concept trial
- Announced positive result from planned interim analysis ($p<0.0001$). Ending enrollment and accelerating development
- Data on full set of subjects expected in 3Q 2022

PRISM

Pruritus Relief through Itch-Scratch Modulation

Pruritus Associated with Prurigo Nodularis



- Completed enrollment January 31, 2022
- Data expected in 2Q 2022
- FDA Fast Track designation granted for moderate to severe pruritus in PN

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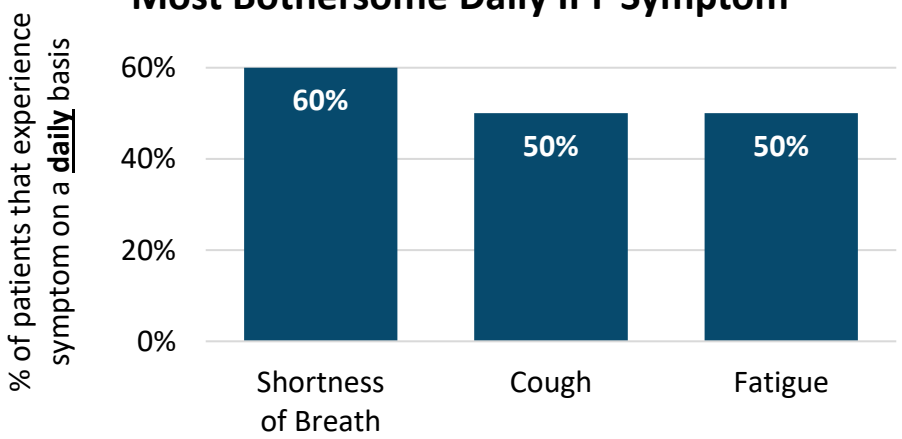
HADUVIO™ (nalbuphine ER) is an investigational drug

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[4]

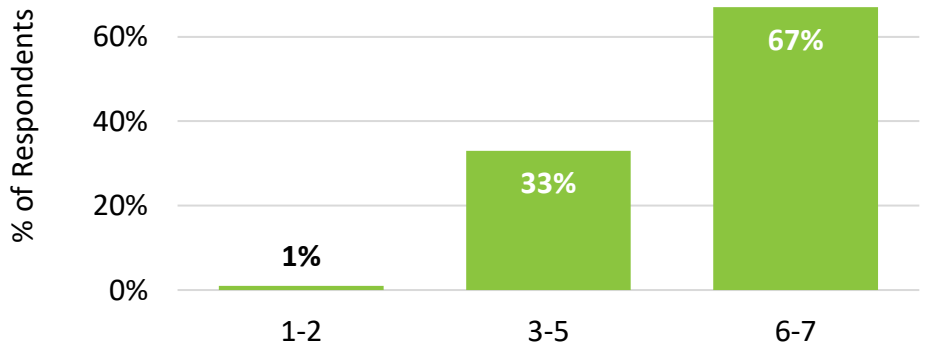
Most Bothersome Daily IPF Symptom[1]



Pruritus Associated with 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)



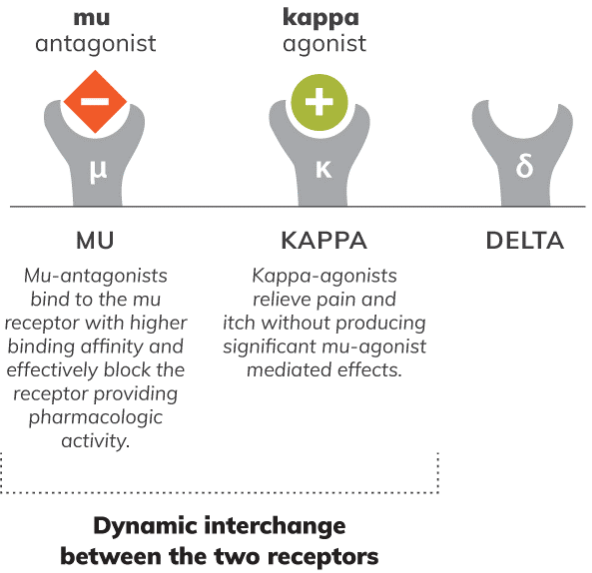
1=no impact at all, 7=very significant impact

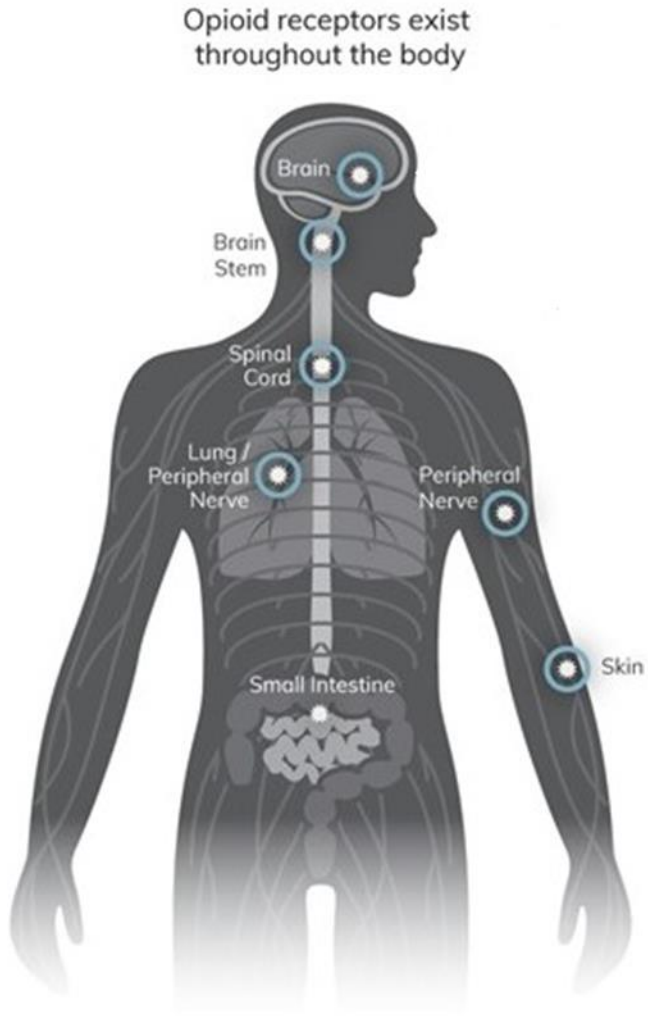
[1]Voice of the Patient – IPF Patient-focused Drug Development Initiative, 2015 [2]Iking A JEADV 2013 [3]Vaidya DC & Schwartz RA Acta Derm Croat 2008 [4]Trevi data on file

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 Cough in Idiopathic Pulmonary Fibrosis (IPF)

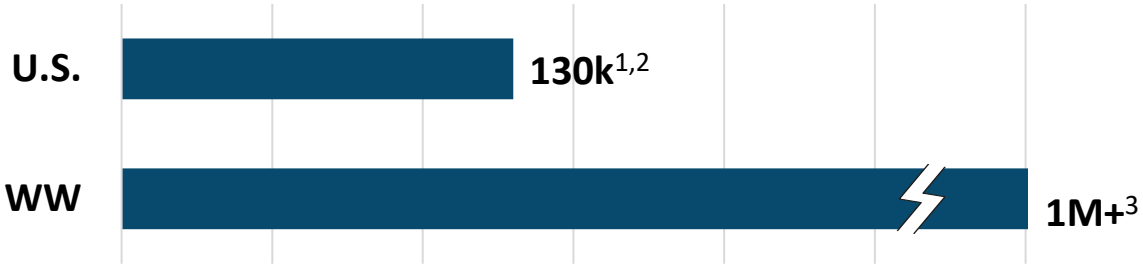
nalbuphine ER Demonstrated Highly Statistically Significant Reduction of Chronic Cough In Idiopathic Pulmonary Fibrosis (IPF) From Ph2 Interim Analysis

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



~85%

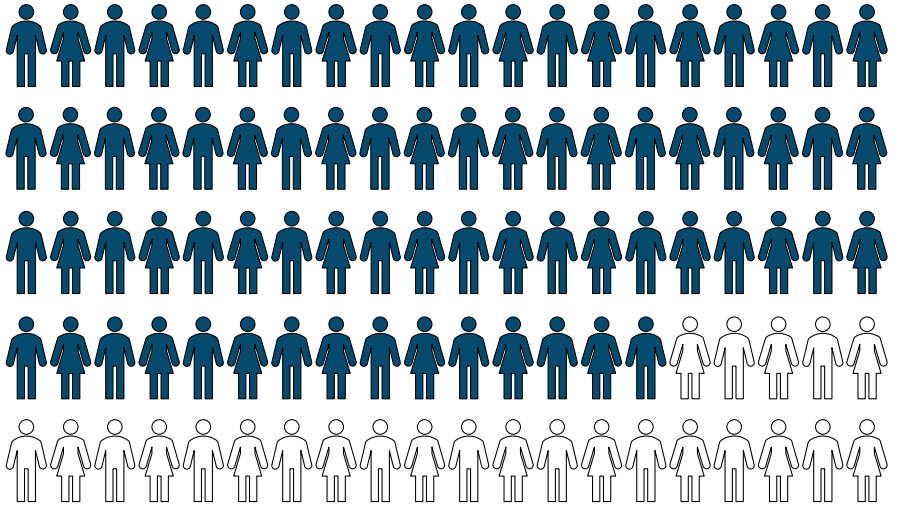
of IPF patients suffer from chronic cough[4]

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

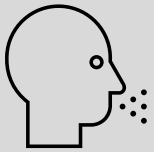
≥75%

of IPF patients report cough as being one of their most significant symptoms[5]



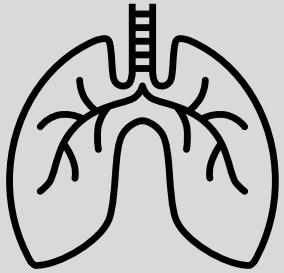
[1]Raghu G et al. Eur Resp J 2016 [2]Raghu G et al. Am J Resp Care Med 2006 [3]Nalsnyk L et al. Eur Resp Rev 2012 [4]Ryerson CJ et al. Respirology 2011 [5]Voice of the Patient – IPF Patient-focused Drug Development Initiative, 2015

The Significant Role of Chronic Cough in IPF



226-520

Median coughs per day of an IPF patient.[1,2] The urge to cough cannot be relieved by coughing.[3]



Marker of Disease

Cough may be an early clinical marker of disease activity, identify patients at high risk of progression, and may predict time to death or lung transplantation.[4]

Refractory

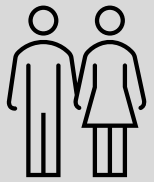
Frequently refractory to antitussive therapy.[5]

Profibrotic

One could hypothesize that cough is not only a symptom but may also contribute to enhanced activation of profibrotic mechanisms and disease worsening in IPF.[6]

Social Interruption

The social impact of chronic cough in IPF further compounds limited exercise ability, reduced walking distance and the need to use supplemental oxygen.[3,7]

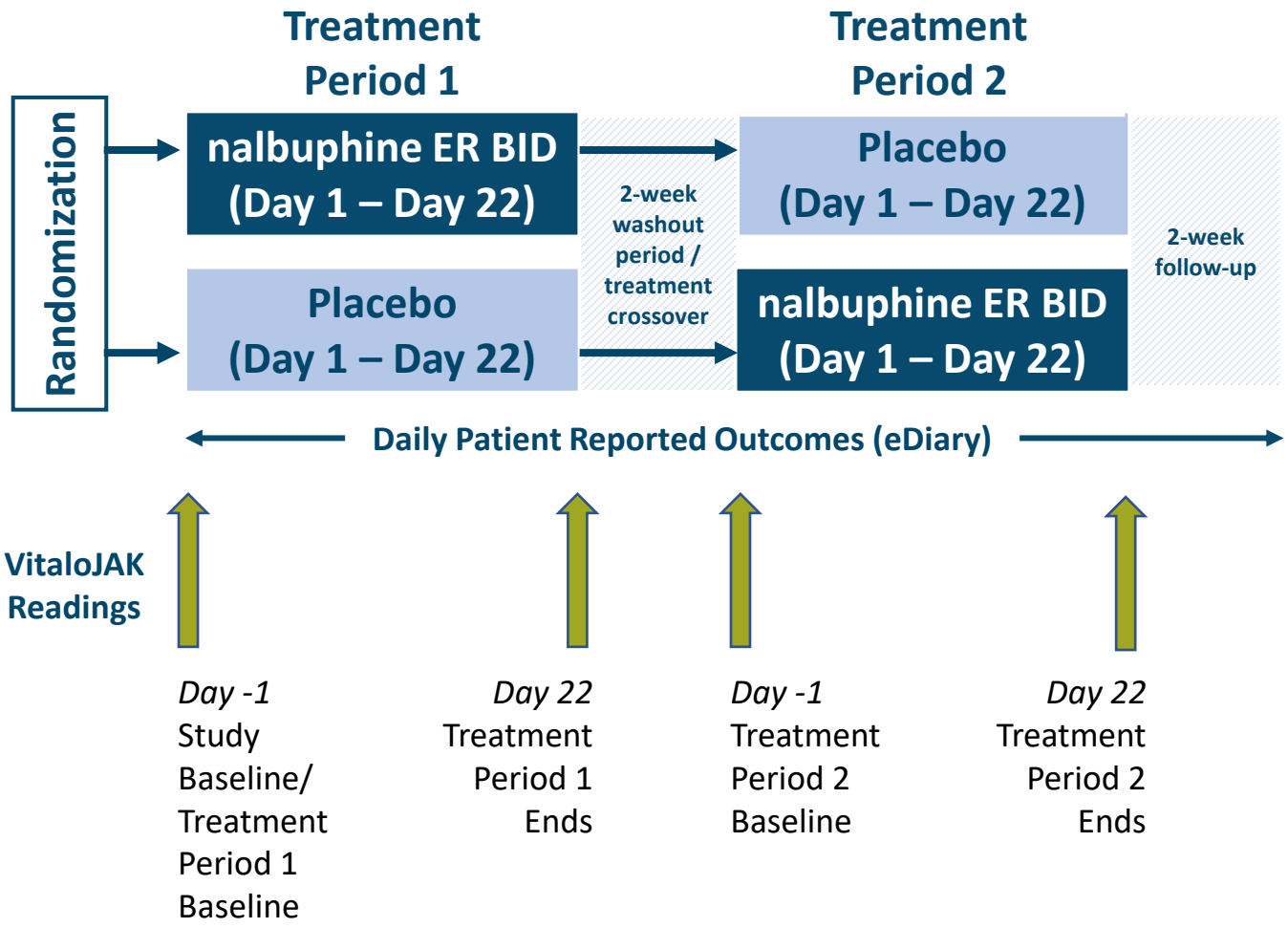


Impacts Daily Function

Coughing can increase feelings of anxiety as it induces breathlessness. Coughing spells or episodes lead to significant fatigue, air hunger, peripheral oxygen desaturation and some patients also experience cough-related urinary incontinence[8,9,10]

[1]Key AL et al. *Cough* 2010 [2]VanManen M et al. *Am J Respir Crit Care Med* 2015 [3]Swigris JJ et al. *Health Qual Life Outcomes* 2005 [4]Ryerson CJ et al. *Resp* 2011 [5]Hope-Gill BDM et al. *Am J Respir Crit Care Med* 2003 [6]VanManen M et al. *ERS* 2016 [7]Key AL et al. *Cough* 2010 [8]vanManen M et al. *Ther Adv Respir Dis* 2017 [9]Wakwaya Y et al. *Chest* 2021 [10]Bradia F et al. *Rev Mal Respir* 2009

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

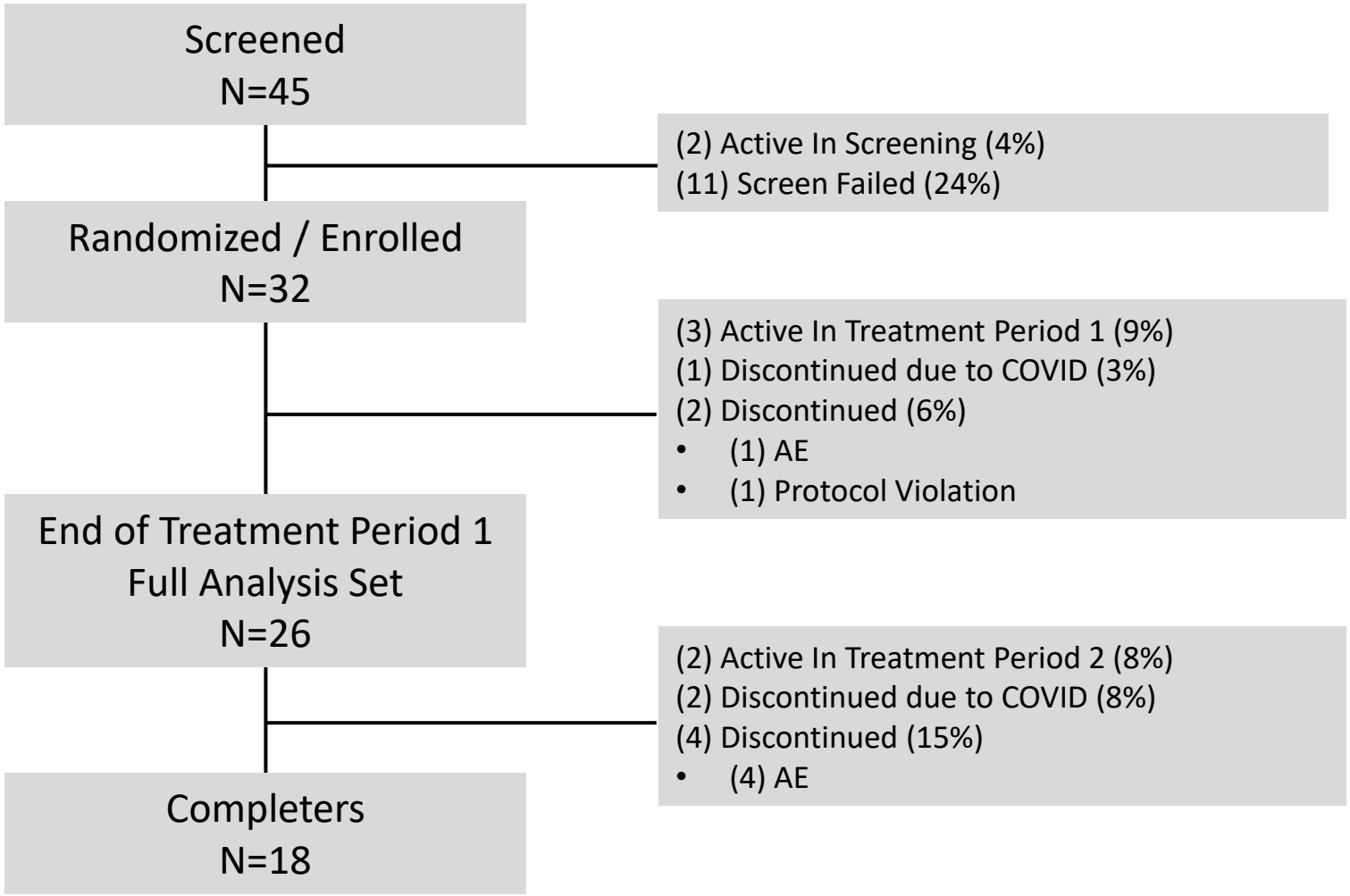
Cough severity
Fatigue
Dyspnea

NALBUPHINE ER

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

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

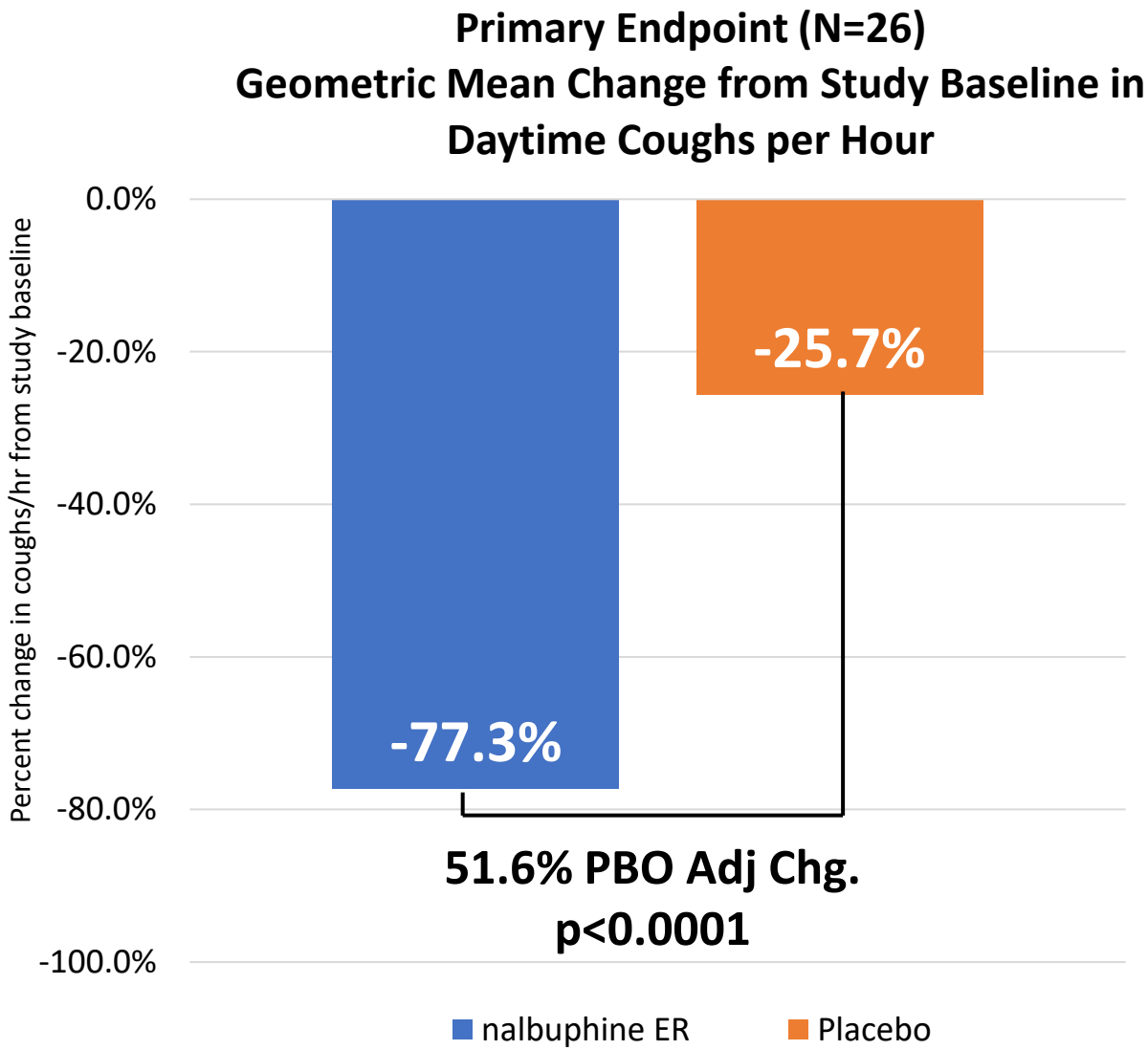
CANAL Interim Analysis Subject Disposition
Data Cut-off: 28 JAN 2022



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

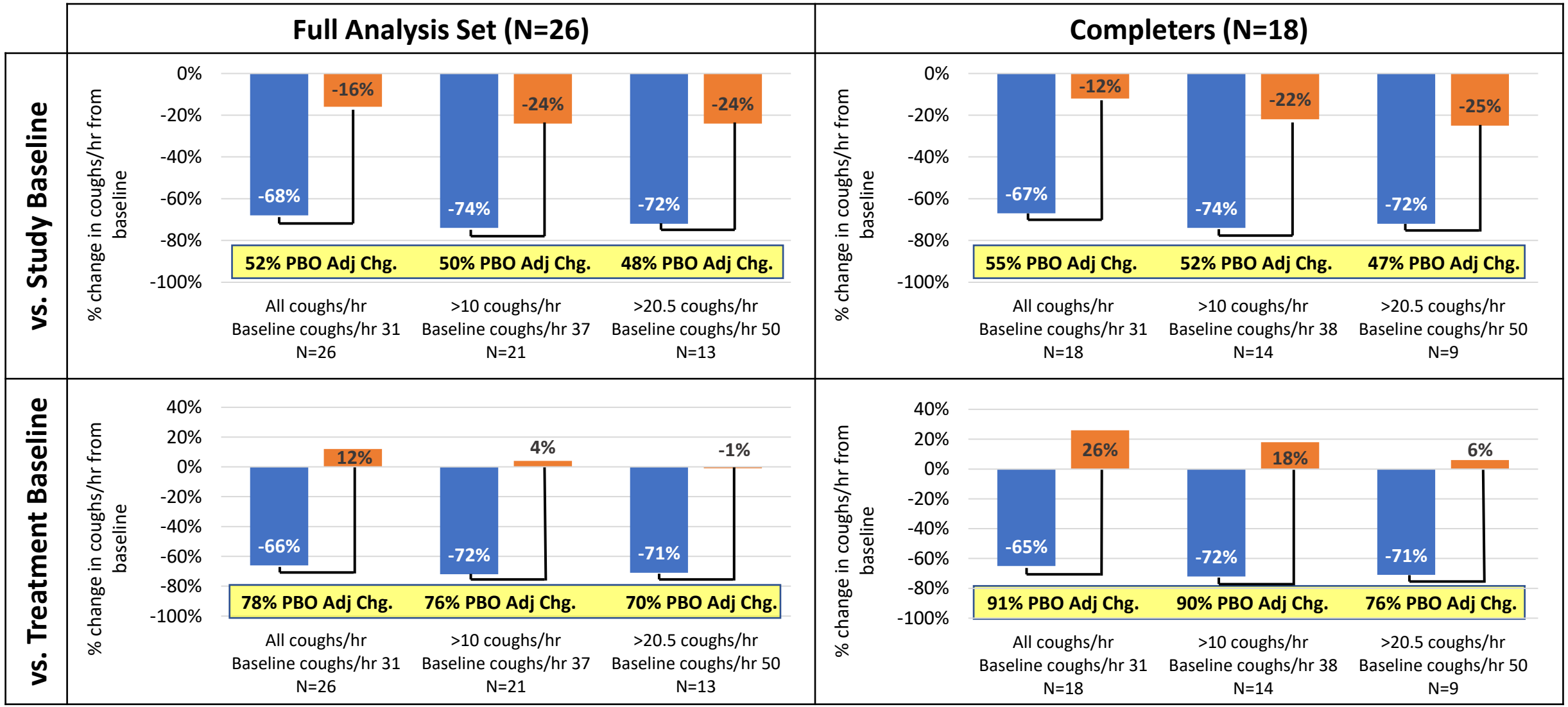


The VitaloJAK® Cough Monitor provides a fully validated system for objective measurement of cough.

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

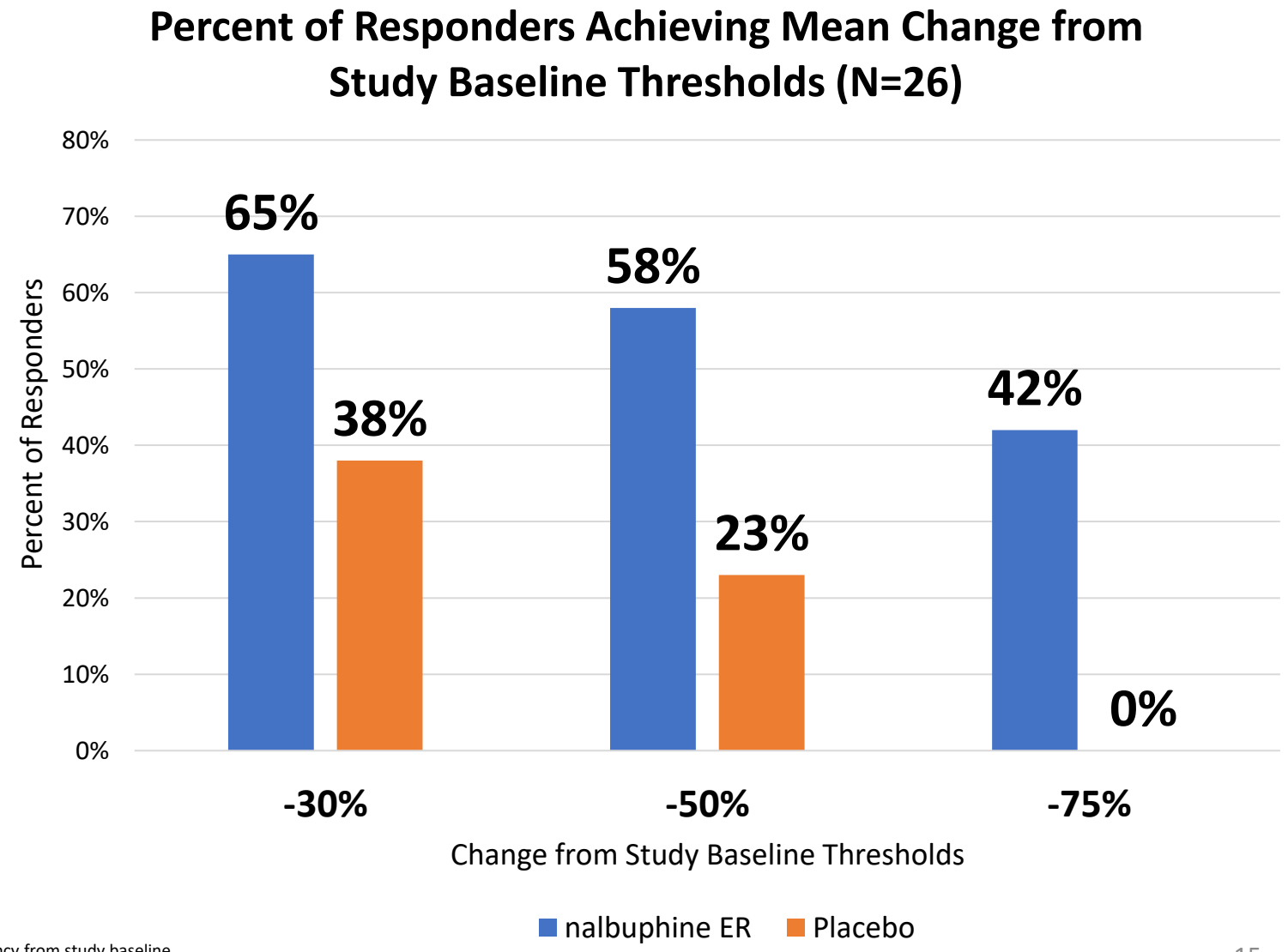
nalbuphine ER Placebo

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 ranged from 30% to 75% improvement

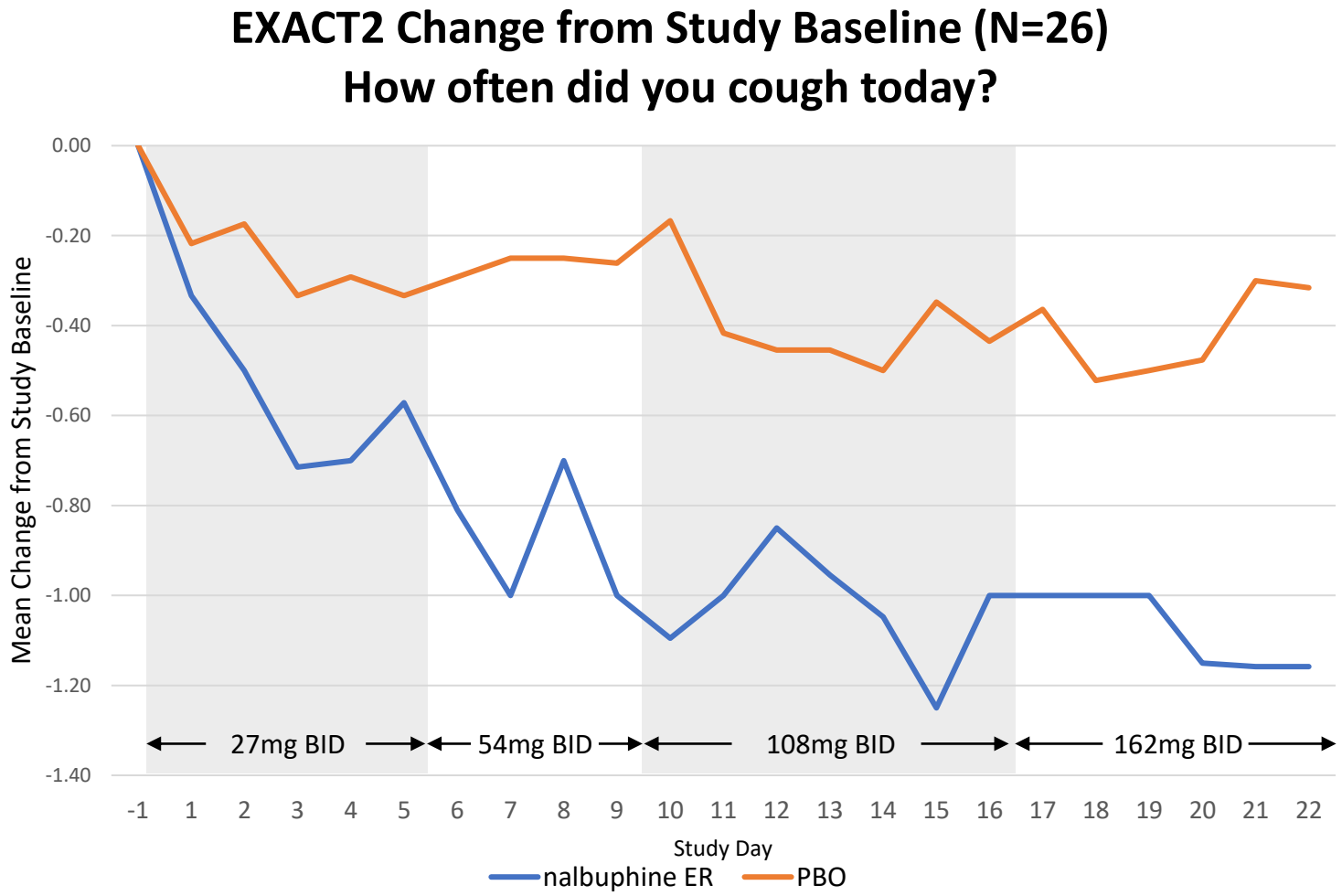
nalbuphine ER outperforms placebo in each analysis

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

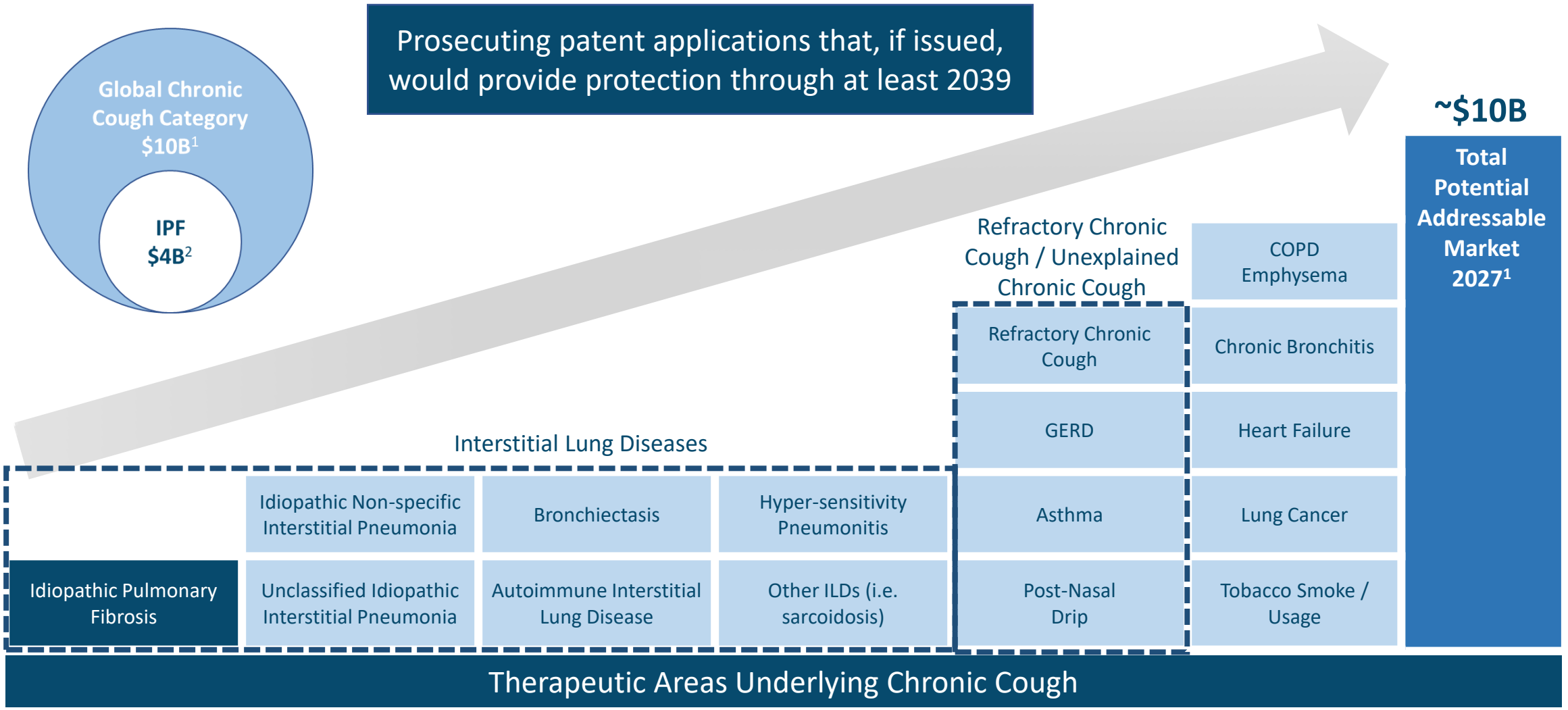
No new safety-related issues have arisen in the study and the adverse event profile of the drug in the IPF subject population is consistent with the safety profile noted in all other past studies where nalbuphine ER has been investigated in a variety of medical conditions

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

Clinical Development Next Steps—IPF Chronic Cough

- 2H 2022: Design proposed Ph 2b/3 study and discuss development plan with relevant health authorities
- 3Q 2022: Complete analyses and report topline data for full set of subjects
- 1H 2023: Prepare to initiate Ph 2b/3 study

Chronic Pruritus in Prurigo Nodularis

PRISM
Pruritus Relief through Itch-Scratch Modulation

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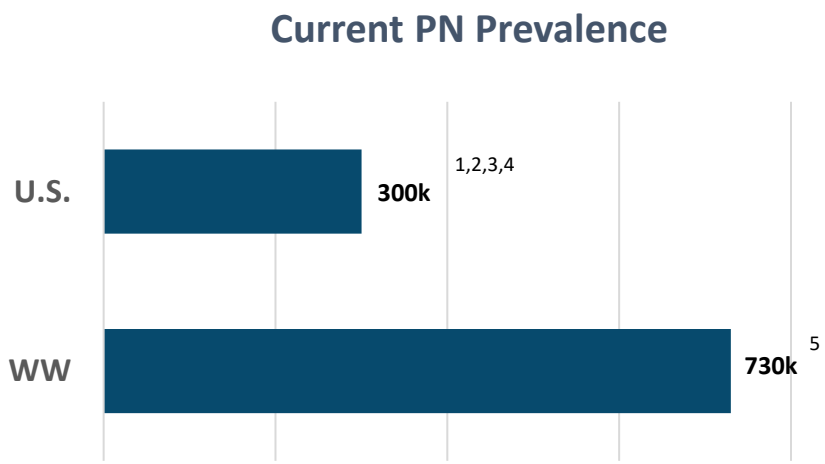
Opportunity to be the First Oral Therapy Approved in Pruritus Associated with Prurigo Nodularis

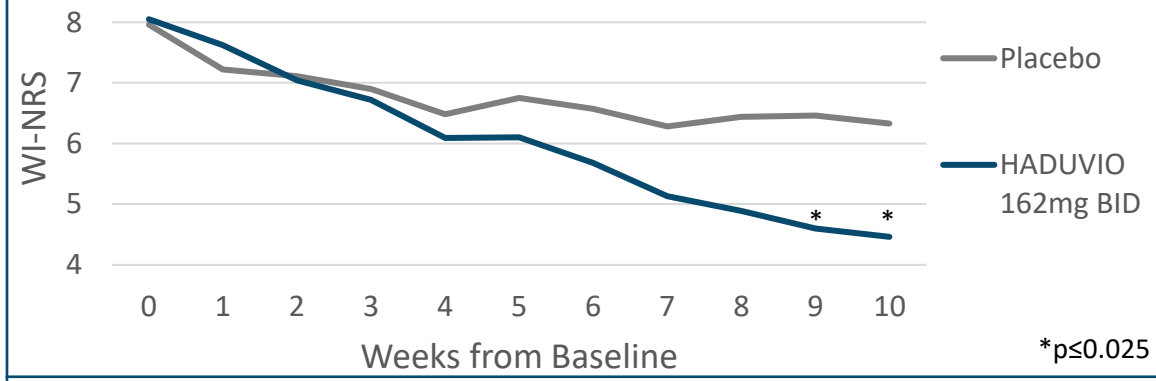


- Current off-label treatments for itch lack efficacy and/or have an unfavorable AE profile
  - We believe 40-50% of patients are uncontrolled on off-label therapies
- Oral therapy enables opportunity to be used in earlier lines of therapy
- Many underlying etiologies of itch, but initial scratching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

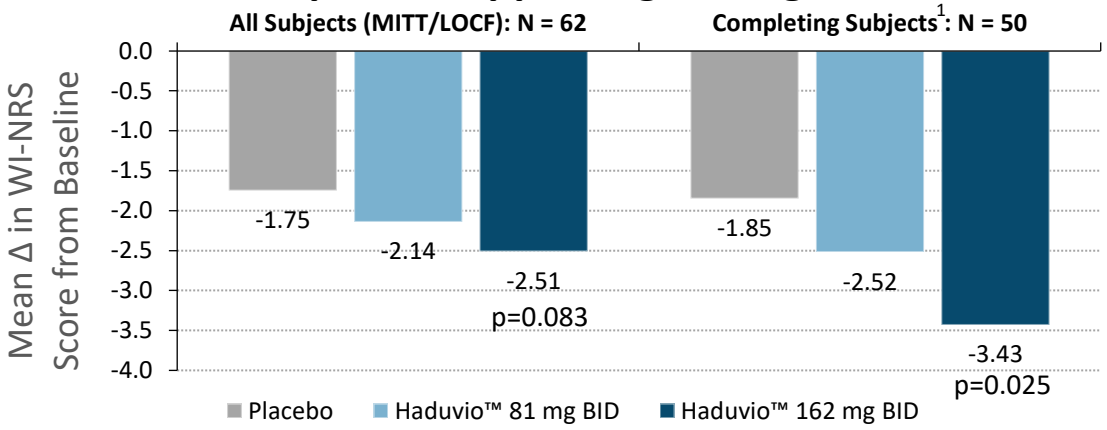
[1]Huang AH JID 2020 [2]Stander S JAAD 2020 [3]Iking A JEADV 2013 [4]Pereira M JEADV 2018 [5]Prurigo Nodularis - Market Insights, Epidemiology and Market Forecast [6]Eigelshoven CME Derm 2009 [7]Vaidya DC & Schwartz RA Acta Derm Croat 2008 [8]Lee MR, Shumack S Aus J Derm 2005 [9]Iking A JEADV 2013

Results from Ph2a Prurigo Nodularis Trial and Open Label Extension (OLE)

Continued Separation of WI-NRS Over Time

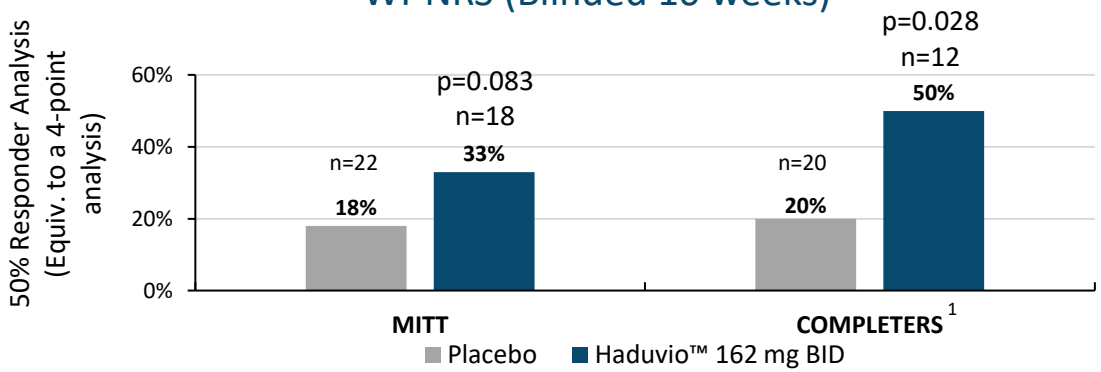


Dose Response Supporting 162mg Selection†



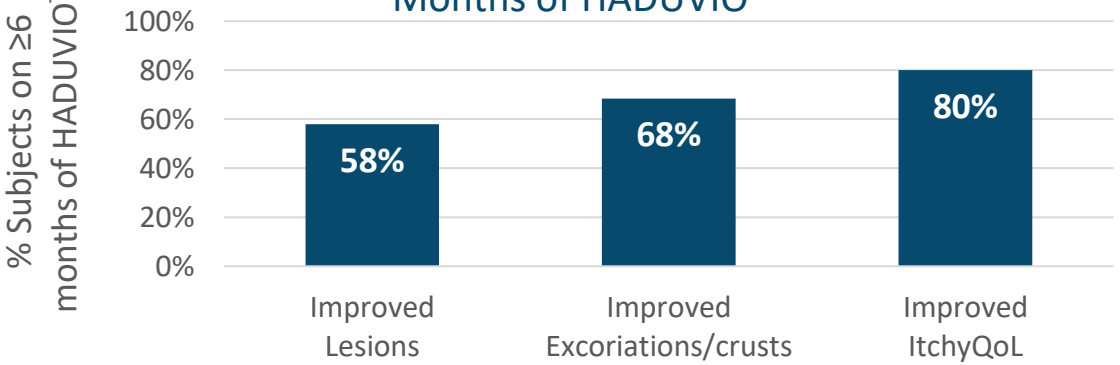
Drug Separation vs. PBO

PN Ph2a 50% Responder Analysis (N=63)
WI-NRS (Blinded 10 weeks)



(OLE) HADUVIO™ Showed Disease Improvements

Percent of Subjects Achieving Outcomes on ≥6 Months of HADUVIO™

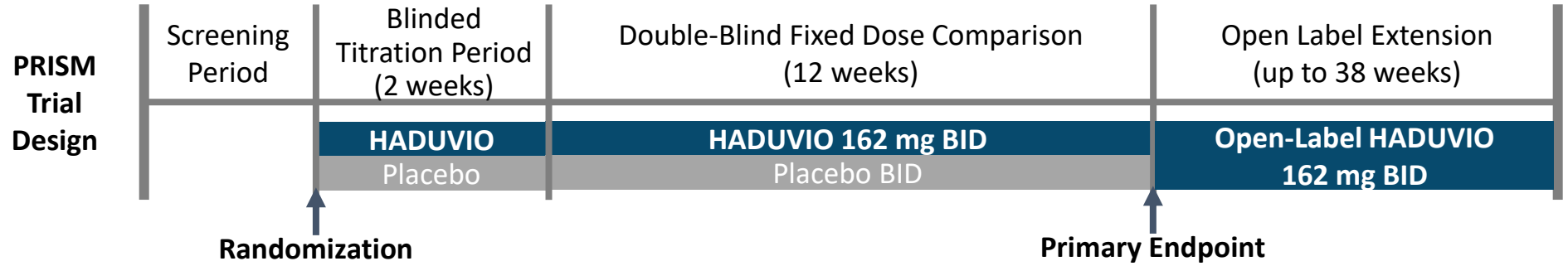


†All p-values compare treatment group to placebo. Only the primary endpoint [30% responder analysis] was powered for statistical significance.
[1]Post-hoc analysis on completers. Consists of the subjects who completed the 10-week course of treatment.
DOI: **10.1111/jdv.17816**
Haduvio (nalbuphine ER) is an investigational drug

Phase 2b/3 PRISM Trial Design (N=~360)

Top-Line Data Expected 2Q 2022

Optimizations from Ph2a to Ph2b/3 PRISM Trial		
Increased Powering	**Enriched Population**	**Increased Duration**
63 subjects (Ph2a) → 360 subjects (Ph2b/3)	Focusing on severe population WI-NRS ≥5 (Ph2a) → WI-NRS ≥7 (Ph2b/3)	10 weeks (Ph2a) → 14 weeks (Ph2b/3)



Trial Status:
- 60+ Sites
- Completed enrollment January 31, 2022

Inclusion Criteria:
- Worst-Itch Numerical Rating Scale (WI-NRS) Score ≥7
- 10+ pruriginous nodules
- PN present on at least 2 separate body parts

Primary Efficacy Endpoint (responder analysis):
- % WI-NRS Responders for NAL-ER versus PBO
- Responder = 4-point reduction from baseline at Wk 14

Key Secondary Endpoints (change from baseline):
- QoL (ItchyQoL)
- Skin lesions
- Sleep disturbances

Open Label Extension:
- ~90% of subjects who reached Wk 14 have continued into the open label extension
- Long-term safety
- Durability of effect
- Lesion healing

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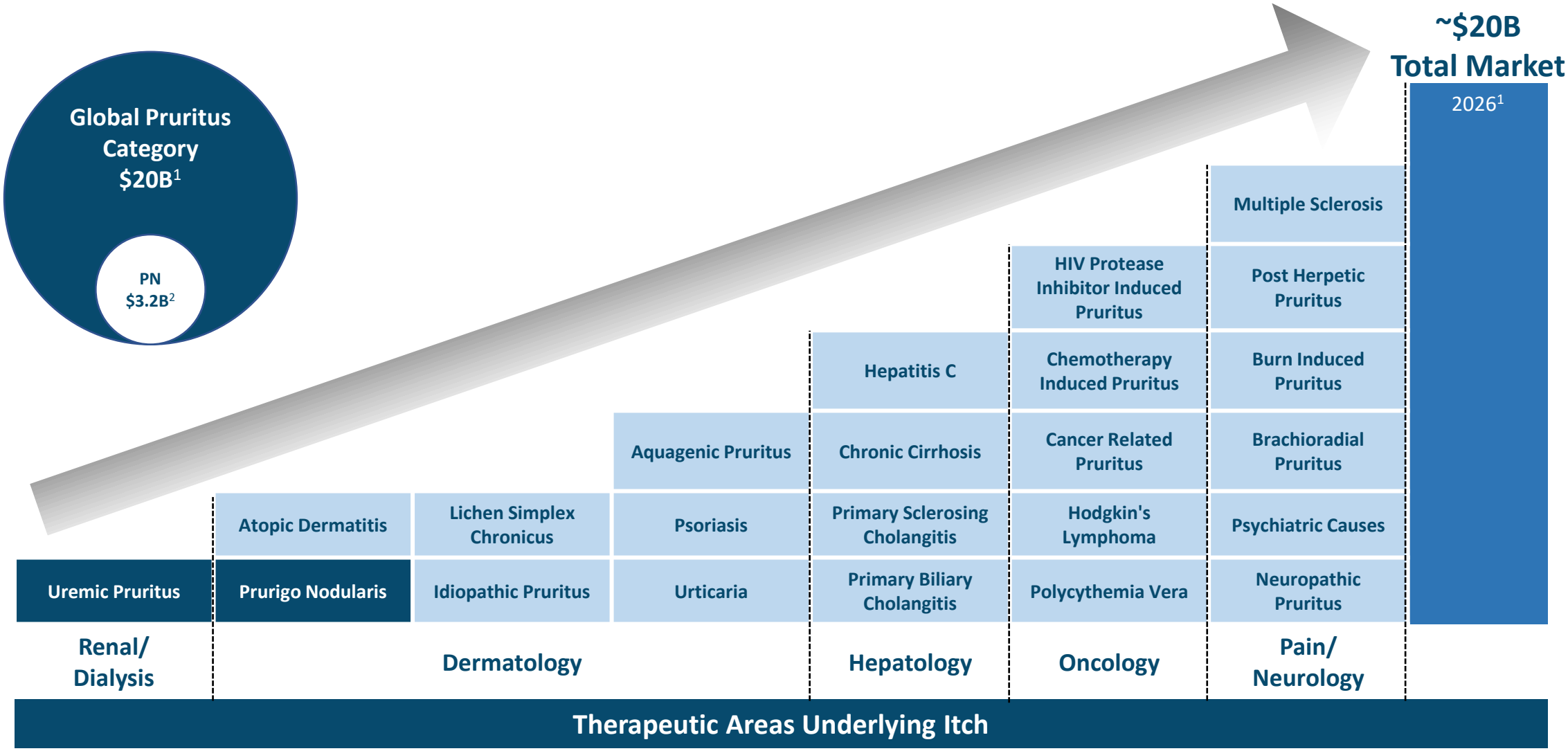
Haduvio (nalbuphine ER) is an investigational drug

Potential Market Opportunity Across a Broad Array of Chronic Pruritic Conditions



[1]2026 est. OG Analysis Global Pruritus Therapeutics Market [2]2031 est. DelveInsight Prurigo Nodularis Market Insight, Epidemiology, and Market Forecast May 2020

Strong Financial Foundation to Advance Pipeline

- **Strong Cash Position**
  - ~$80M in pro-forma cash position as of April 11, 2022
    - $55M PIPE executed at market with Frazier, Venrock, Fairmount and NEA (existing investor)
  - ~82M fully diluted shares outstanding
    - Includes 18M warrants that will generate an additional $25M in cash when exercised

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

- **Cash runway into Q1 2024**

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Trevi Value Proposition

Rebalancing the Cough/Itch Pathway	Dual acting MOA in clinical development that works both peripherally and centrally to rebalance the kappa and mu receptors, both of which are important in mediating cough and pruritus
Strong Cough in IPF Interim Results	Chronic cough Ph2 interim analysis showed 52% placebo-adjusted reduction in daytime cough frequency ($p \leq 0.0001$) Potential to be first in class and best in class therapy for cough in IPF
Near Term Data for Lead Indications	Pruritus in PN Ph2b/3 topline data expected 2Q 2022 Chronic cough in IPF Ph2 topline data expected 3Q 2022
Broad Potential Use Across Therapeutics Areas	Ability to utilize nalbuphine ER across a variety of therapeutic areas that experience cough and itch
Strong Cash Position	Approximately $80m in cash Current runway estimated into Q1 2024