Bellerophon Therapeutics

Company Presentation | March 2021

Bellerophon THERAPEUTICS

Forward Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make due to a number of important factors, including risks and uncertainties relating to: INOpulse® not proving to be an effective treatment for COVID-19 or approved for marketing by the FDA, the timing and outcomes of our ongoing and expected clinical trials for our product candidates; our ability to successfully develop, commercialize and market any of our product candidates; our ability to obtain, maintain and enforce intellectual property rights; competition; our reliance on third parties; our ability to obtain necessary financing; and those risk factors discussed in the "Risk Factors" section and elsewhere in our most recent Form 10-K and other periodic filings we make with the SEC.

All forward-looking statements contained in this presentation reflect our current views with respect to future events. We assume no obligation, except as required by applicable law, to update any forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

Bellerophon Therapeutics (BLPH) Company Profile

Clinical-Stage Biotherapeutics Company

- Focused on developing inhaled nitric oxide (iNO) based therapies for management of serious cardiopulmonary diseases
- Portable, lightweight delivery system (INOpulse®) allows for chronic home use
- Simplified regulatory approval pathway via existing nitric oxide NDA
- Company spun-off from Ikaria

Novel Therapy Addressing Unmet Medical Needs

- Multiple late stage programs in respiratory diseases including fibrotic ILD, and pulmonary hypertension
- Novel targeted vasodilation provides potential for first approved therapy in multiple indications

Financial Summary

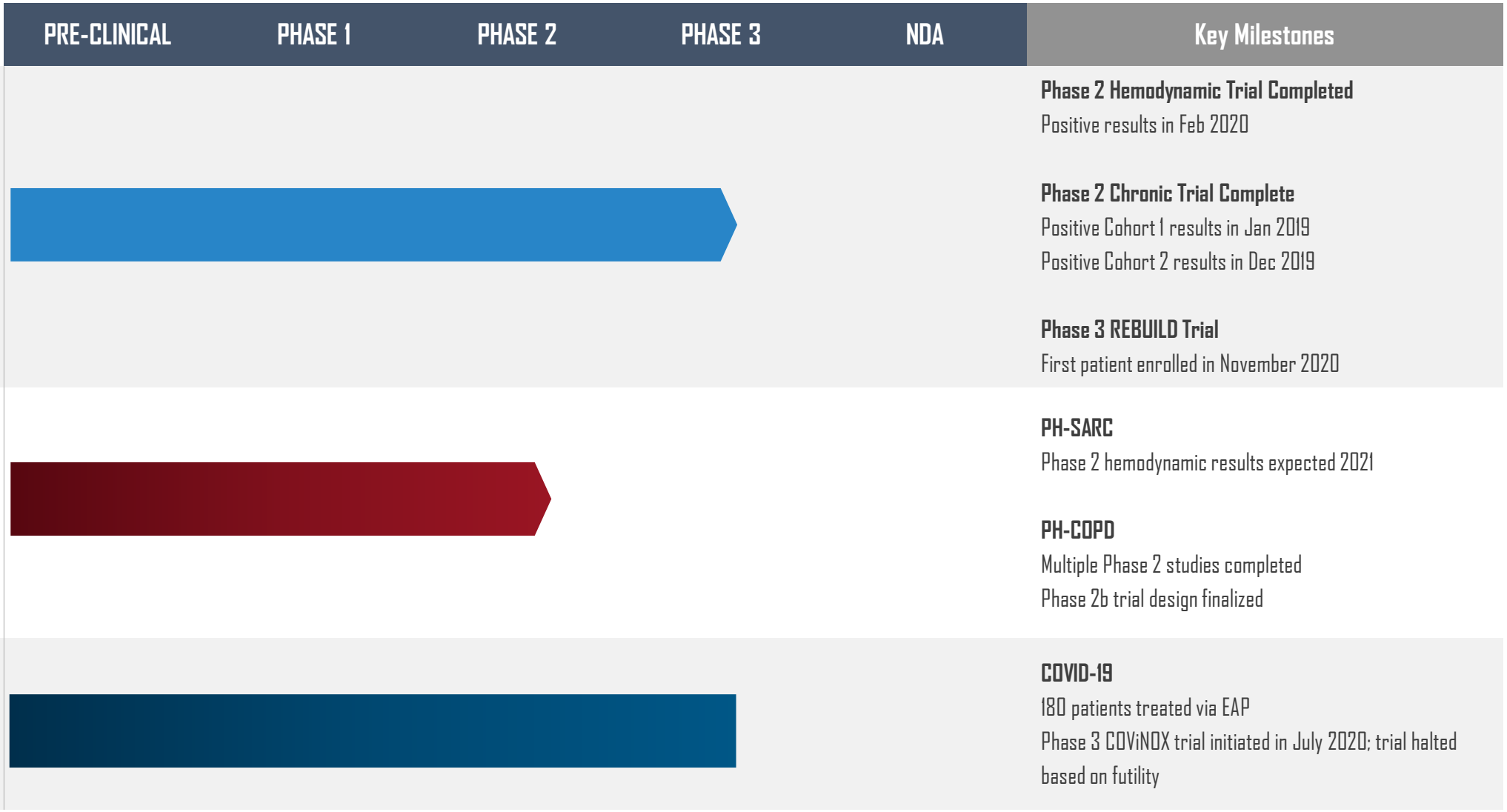
- Cash & Equivalents: $47.6 M[1]
- No Debt[1]
- Fully Diluted Shares Outstanding = 12.2 million

1. As of December 31, 2020

Highly Experienced Leadership Team

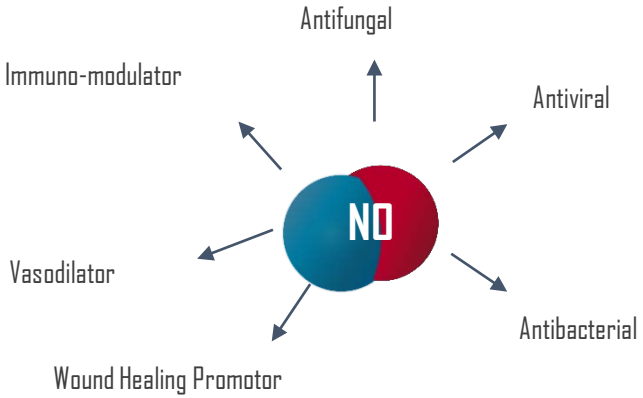
Jonathan Peacock Chairman	**10 years** experience as CFO at Amgen and Novartis Pharma	AMGEN, McKinsey&Company, NOVARTIS, pwc
Fabian Tenenbaum Chief Executive Officer	**15 years** of executive-level experience in finance, BD and operations	anterios, Unilever, SYNERON CANDELA
Edwin Parlsey, D.O. Acting Chief Medical Officer	**31 years** experience in clinical research specializing in cardio-pulmonary diseases	LIQUIDIA CORPORATION, respira therapeutics, Pfizer, UTHealth The University of Texas Health Science Center at Houston
Peter Fernandes Chief Regulatory & Safety Officer	**25 years** experience in global regulatory affairs specializing in respiratory products	IKARIA, NOVARTIS, Boehringer Ingelheim
Assaf Korner Chief Financial Officer	**18 years** of financial experience in medical device and life science companies	SYNERON CANDELA, KPMG, Unilever
Parag Shah, Ph.D. VP, Business Operations	**15 years** experience in pharmaceutical product development	IKARIA, Pfizer
Amy Edmonds VP, Clinical Operations & Administration	**20 years** experience global clinical operations and training	IKARIA, Pfizer, Celgene
Martin Dekker VP, Device Engineering & Manufacturing	**17 years** experience in new product development and launch	SPACELABS HEALTHCARE

Development Pipeline



INOpulse Delivery System Overview

Portable Delivery System Allows Chronic iNO Therapy



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INOpulse®

Nitric Oxide

Well-established vasodilator approved for acute treatment of persistent pulmonary hypertension in hospitals

Portable pulsatile iNO delivery system

Proprietary algorithm ensures accurate dosing independent of patient's breath rate and tidal volume

Portable stand-alone system allows for out-patient treatment

Novel drug-device combination therapy with multiple mechanisms of action

Targeted pulmonary vasodilation

Ventilation/Perfusion (V/Q) matching

Improved oxygen saturation

INOpulse Delivery System

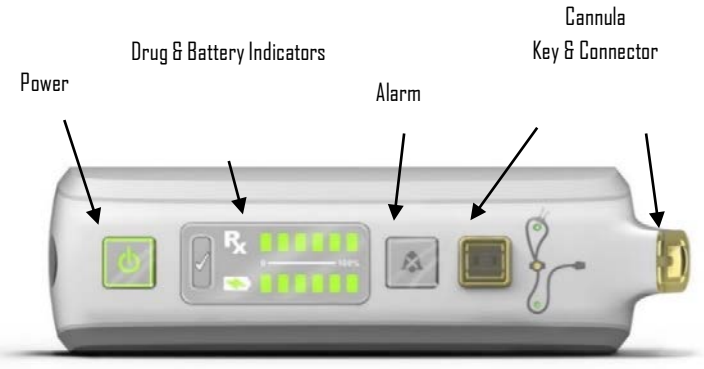
Lightweight, Portable and User Friendly

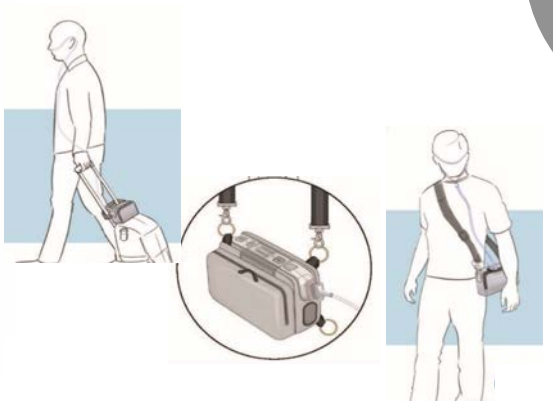
01 Easy engagement with drug cartridge

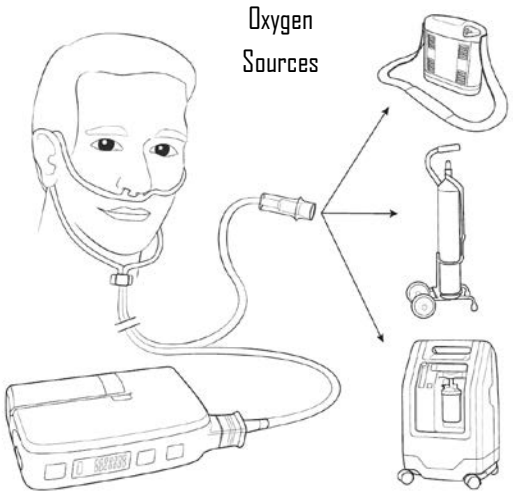
02 Intuitive and simple user interface

03 Tri-lumen cannula allows direct connection with oxygen

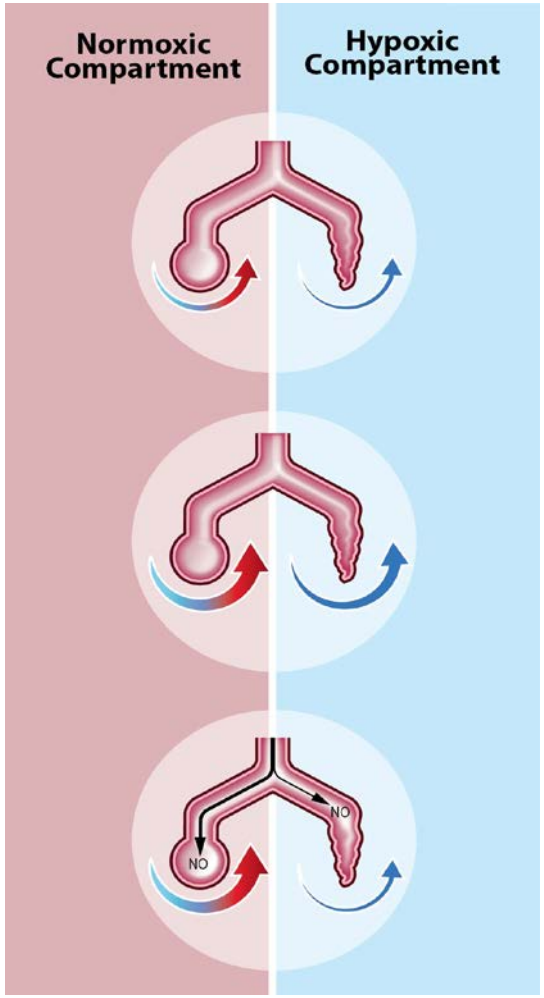
04 Lightweight portable design allows ease of transport







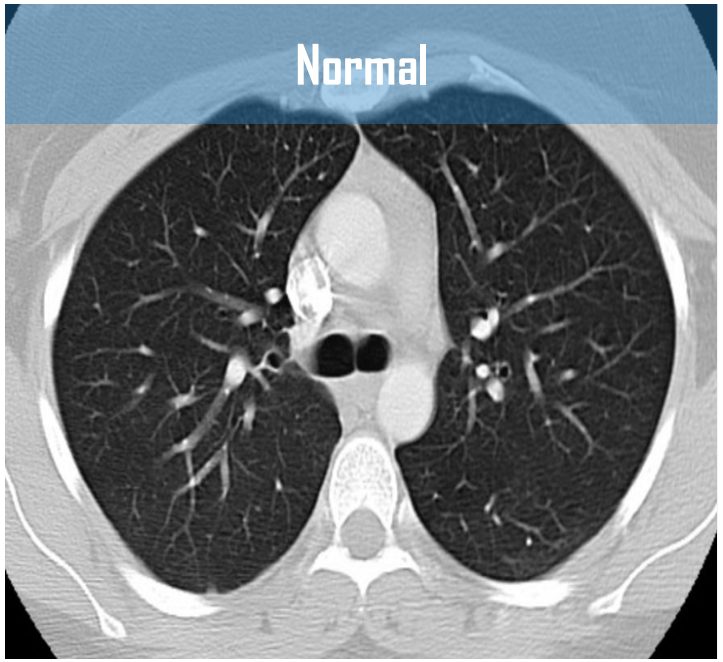
INOpulse Provides a Unique and Differentiating Mechanism of Action

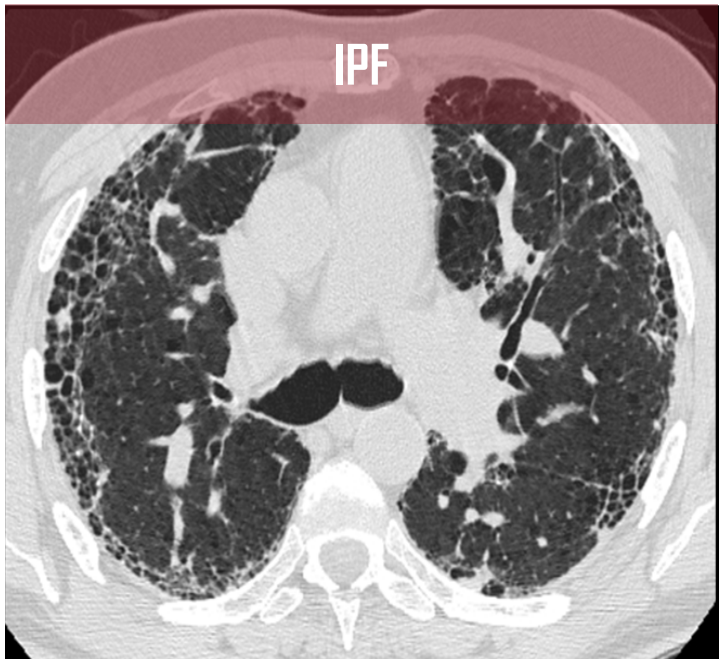


Baseline	Hypoxic pulmonary vasoconstriction prevents oxygen desaturation
Systemic Vasodilators	Systemic vasodilators can reverse hypoxic vasoconstriction leading to ventilation/perfusion (V/Q) mismatch and arterial 02 desaturation
INOpulse	Providing iNO early in the inspiratory phase allows for targeted vasodilation of only the well ventilated alveoli thereby preventing V/Q mismatch and 02 desaturation

Fibrotic Interstitial Lung Disease (fILD)

A Significant Unmet Medical Need

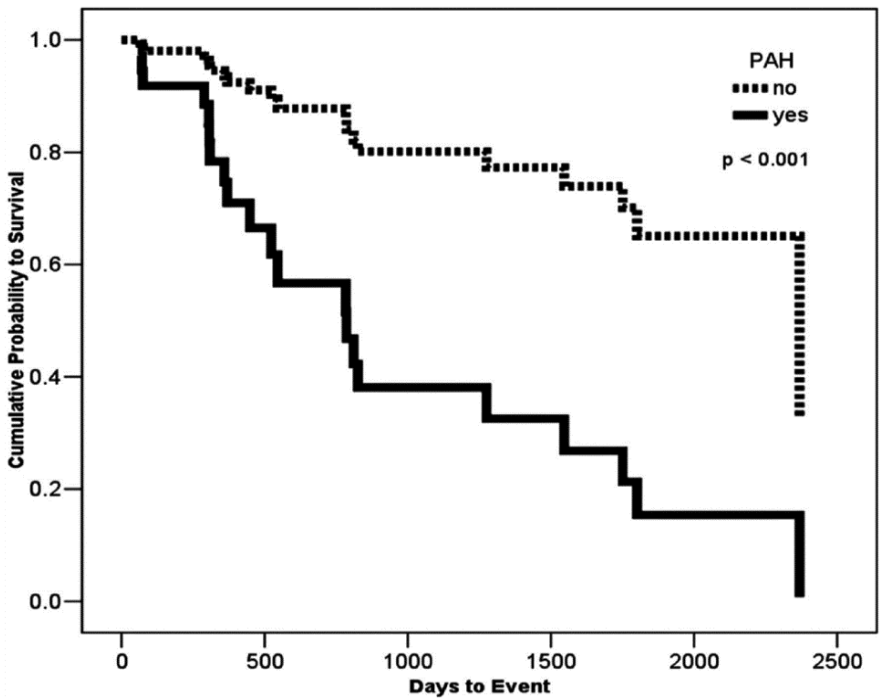




- Fibrotic Interstitial Lung Disease (fILD) is a broad category of diffuse lung diseases characterized by variable amounts of inflammation and fibrosis
- Idiopathic Pulmonary Fibrosis (IPF) is the largest and most serious of these diseases
- Patients with fILD have thickening and scarring of the air sacs in the lungs, and often require supplemental oxygen to maintain adequate oxygen saturation

Pulmonary Hypertension (PH) associated with fILD Significantly Reduces Survival

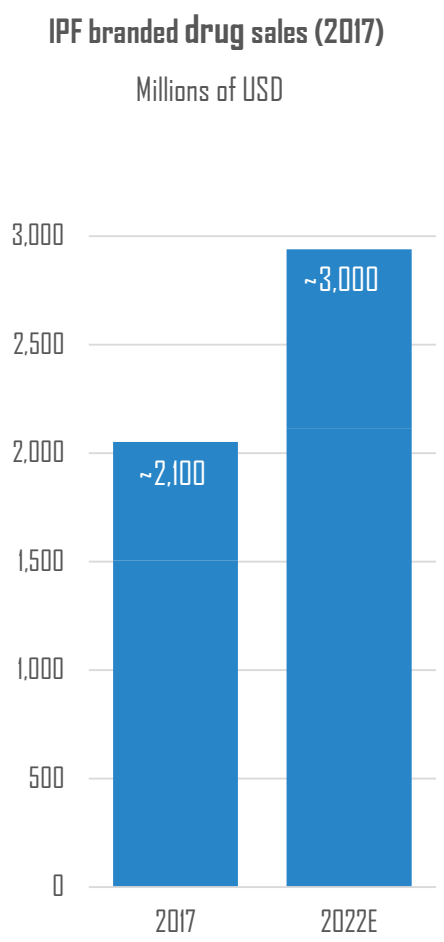
Pulmonary Hypertension as Predictor of Survival in IPF

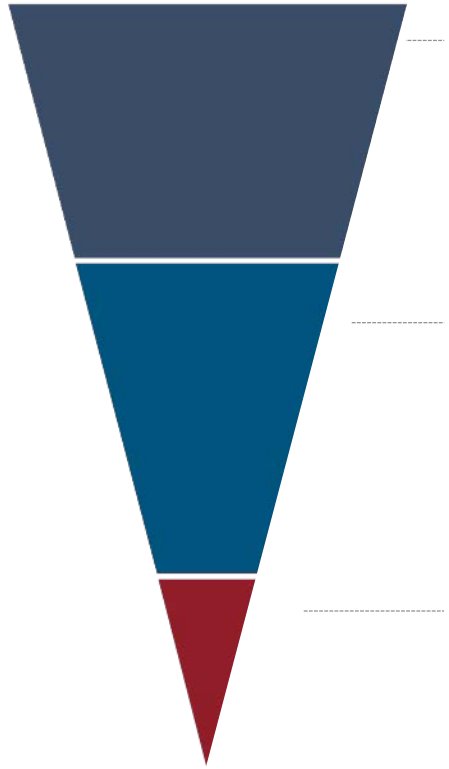


- Approximately 40% of IPF patients exhibit symptoms of pulmonary hypertension at rest
- Prognosis and survival are significantly worse for patients with pulmonary hypertension
- PH-IPF associated with 3-fold increase in risk of death compared to IPF alone
- **No approved therapy for treating PH in these patients**
- INOpulse has the potential to provide targeted vasodilation while avoiding concerns of V/Q mismatch which have prevented current PAH systemic vasodilators to be approved for this unmet medical need

Rivera-Lebron, Advances in Pulmonary Hypertension, 2013

fILD Market Opportunity in the US





fILD Patient Population: ~226,000 in US

Patients would be eligible for INOpulse therapy regardless of verified PH

~44% are IPF (~100,000 in US)

PH-fILD: ~84,000 in US

Estimated patient population with PH at rest (35-40%)

Represents intermediate/high risk of PH by echo

Estimated Penetration: ~24,000 in US Based on:

LTOT penetration of 70-75%

Physician adoption rate of 35-60%

$2B+ US Market Opportunity

KOL feedback supports high unmet medical need in fILD

Pricing assessment supported by current IPF and PAH therapies priced at $100-200k/year

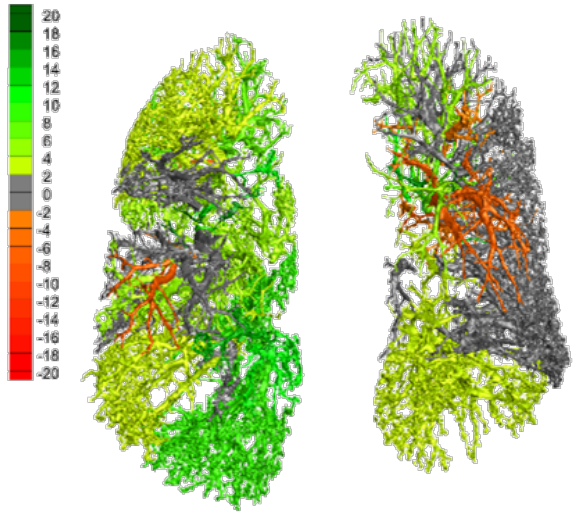
Source: LEK report (2018)

Phase 2: INOpulse Demonstrates Targeted Vasodilation in fILD

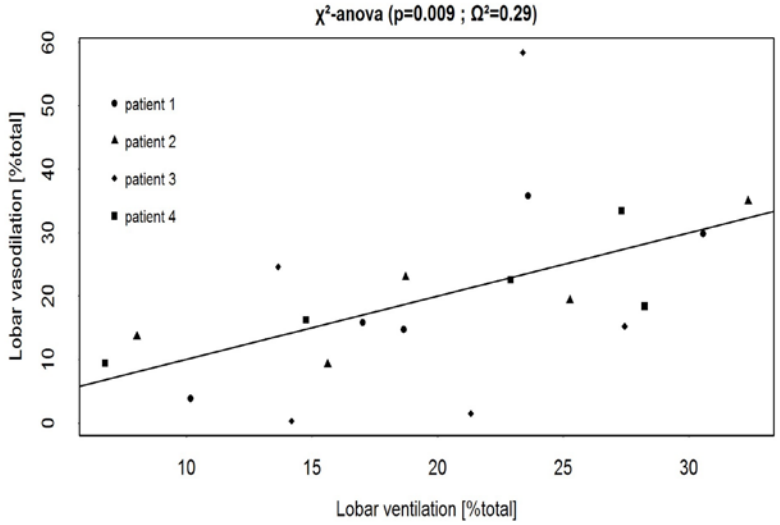
Acute Phase Data Showed Immediate Benefit of INOpulse on Vasodilation and Hemodynamics

- Significant correlation between ventilation and vasodilation, demonstrating selective vasodilation to better ventilated areas of the lung (p=0.009)
- Consistent and clinically meaningful reduction of 14% in systolic pulmonary arterial pressure (sPAP)
- Clinically meaningful improvement oxygen desaturation of 28.5% and SpO2 nadir of 5.5%

Targeted Vasodilation



Ventilation/Vasodilation Matching

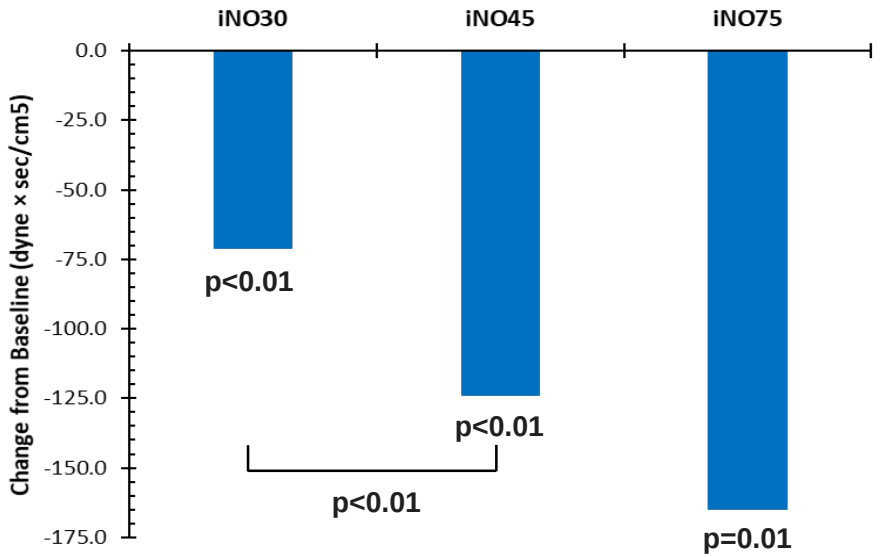


Phase 2: INOpulse Demonstrates Acute Hemodynamic Benefit in fILD

Clinically and statistically meaningful cardiopulmonary improvement on iNO30 with continued benefit on dose escalation

Pulmonary hemodynamics measured via right heart catheterization at baseline and following each sequential iNO dose

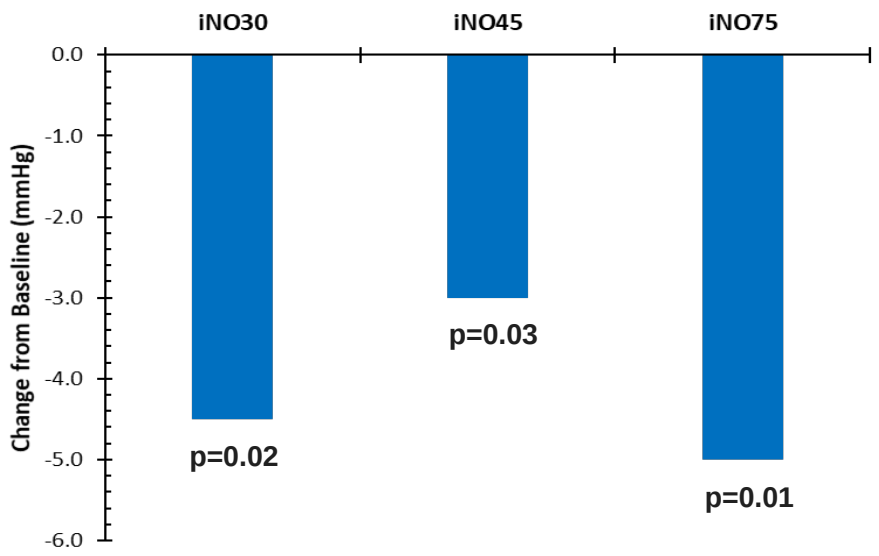
Pulmonary Vascular Resistance (PVR)



Baseline PVR: 583 dyne×sec/cm^5

Average reduction of 125 dyne×sec/cm^5

mean Pulmonary Arterial Pressure (mPAP)



Baseline mPAP: 34.7 mmHg

Average reduction of 4 mmHg

- p-value based on Wilcoxon Rank Test
- Bar graphs are median values at each assessment for all available study participants
- Oxygen saturation remained stable and iNO was well-tolerated with no safety concerns across doses
- Data based on 9 fILD study participants

Continuous Physical Activity Monitoring (Actigraphy) Allows Objective Assessment of Daily Physical Activity

Continuous Monitoring of Physical Activity

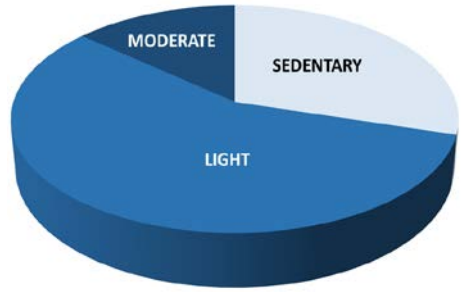
Study participant wears actigraphy monitor on non-dominant arm

Monitor continuously measures movement in acceleration units

Movement is Categorized into Activity Intensity Levels

Activity Intensity	Example activities
Sedentary (<100 counts/min) (< 1.5 METs)	• Lying • Sitting • Computer work
Light (100 -1951 counts/min) (1.6 - 3.0 METs)	• Getting dressed • Bathing/showering • Light house cleaning
Moderate (1952-5724 counts/min) (3.1 - 6.0 METs)	• Walking • Ascending/descending stairs • Housework/yardwork
Vigorous (>5724 counts/min) (> 6.0 METs)	• Slow/fast running • Intense sport

Provides Profile of Daily Activity



Study participants spend 74 minutes per day in moderate physical activity

Study participants are unable to achieve vigorous activity levels

MVPA is the sum of moderate and vigorous activity

Phase 2 Results Suggest Clinically Meaningful Benefit in MVPA (moderate to vigorous physical activity)

Phase 2 was designed as an exploratory study to identify optimal endpoints to progress into pivotal Phase 3 trial. Key findings include:

- Study participants on INOpulse (iNO30 and iNO45) maintain activity levels while study participants on placebo deteriorate across activity parameters
- Study participants on iNO45 maintain PRO scores (UCSD & SGRQ) while study participants on placebo deteriorate consistent with changes in activity levels
- Physical activity levels maintained during open label extension with study participants transitioning from placebo to active demonstrating reversal from decline to maintenance
- INOpulse targeted delivery maintains oxygen saturation during exercise
- INOpulse was generally well-tolerated with no serious adverse events

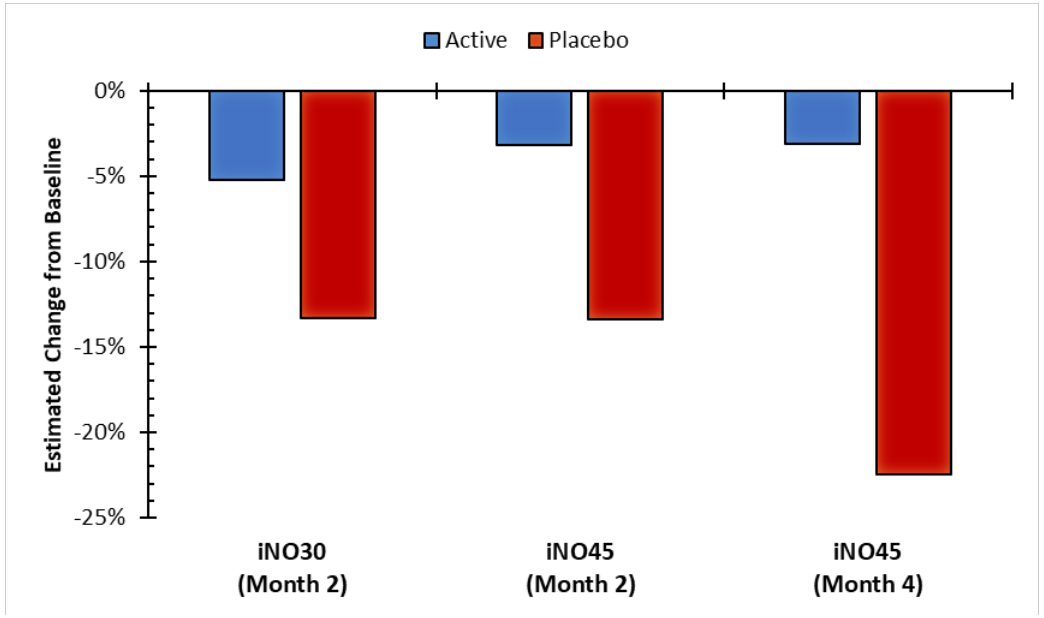
Phase 2 Patient Demographics

	Cohort 1 (n=41)		Cohort 2 (n=44)	
	iNO 30 n=23	Placebo n=18	iNO 45 n=30	Placebo n=14
Age – years (mean, SD)	68.6 (6.45)	65.8 (13.73)	68.9 (9.95)	71.4 (5.14)
Male (n, %)	16 (69.6%)	13 (72.2%)	15 (50.0%)	10 (71.4%)
Intermediate to High Probability of PH (n, %)	15 (65.2%)	14 (77.8%)	18 (60.0%)	9 (64.3%)
Baseline DLCO – % predicted (mean, SD)	30.7 (11.4)	30.4 (10.2)	35.7 (14.2)	35.3 (7.9)
Baseline FVC – % predicted (mean, SD)	56.3 (10.2)	59.9 (18.4)	59.7 (15.9)	60.5 (15.1)

Longitudinal Analysis Benefit on iNO in MVPA and Overall Activity

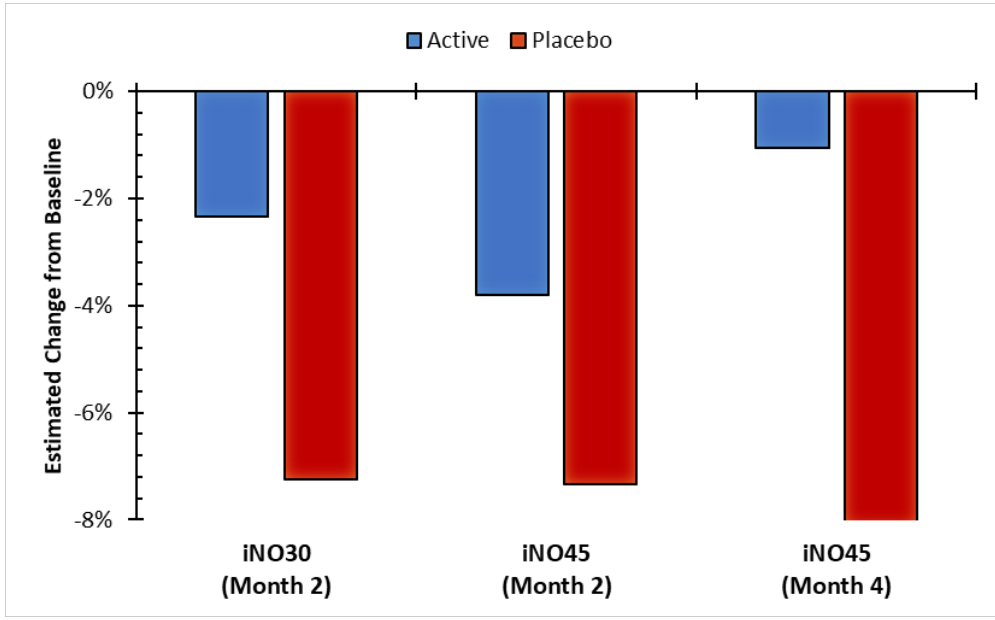
Analysis based on MMRM model to estimate therapeutic benefit through treatment period based on all available data as planned for pivotal Phase 3 study

MVPA



20% benefit after 4 months of treatment

Overall Activity



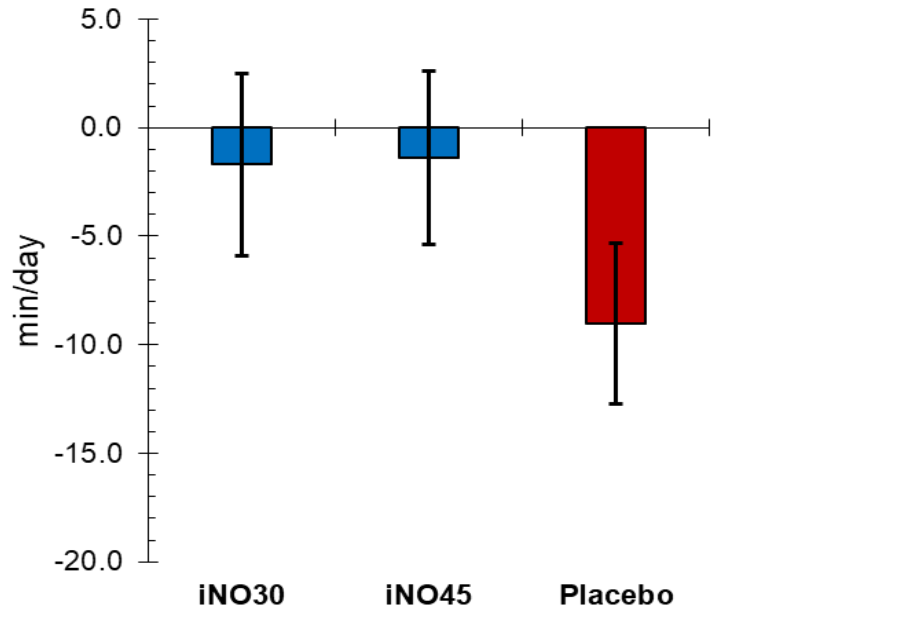
7% benefit after 4 months of treatment

- MMRM model based on change from Week 1 or Month 1; no baseline covariate
- Data log-transformed for normality
- Month 2 data based on pooled placebo and weeks 4-8
- Month 4 data based on months 2-4

Benefit Observed in MVPA at Month 4 on iNO45

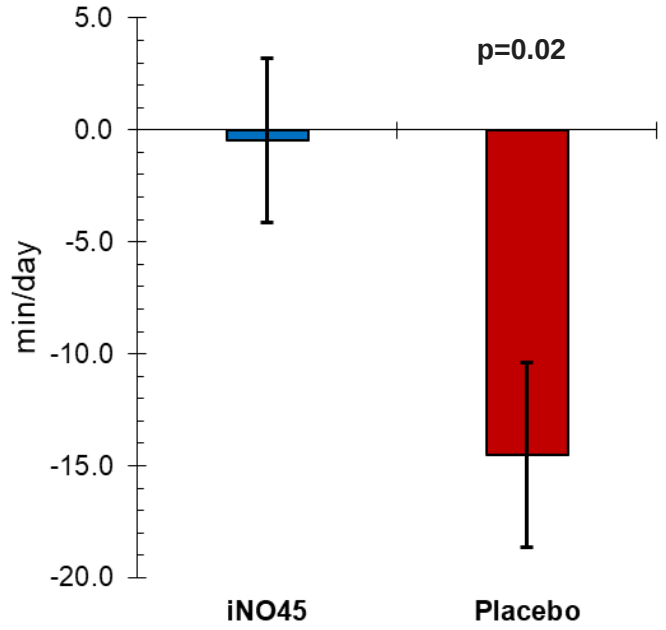
Study participants on INOpulse maintain activity levels while study participants on placebo deteriorate

MVPA Month 2



Study participants on INOpulse demonstrate 7.5 min/day (~10%) benefit over placebo after 2 months of treatment

MVPA Month 4

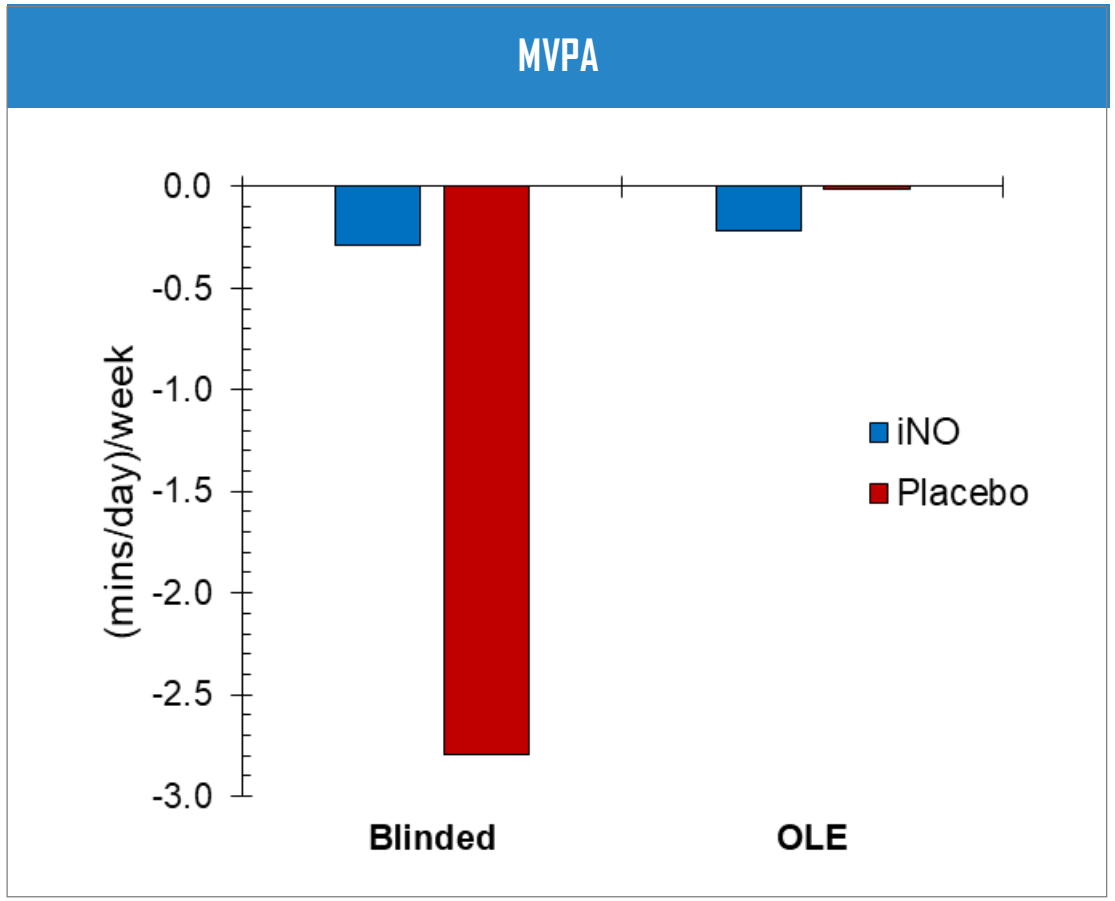


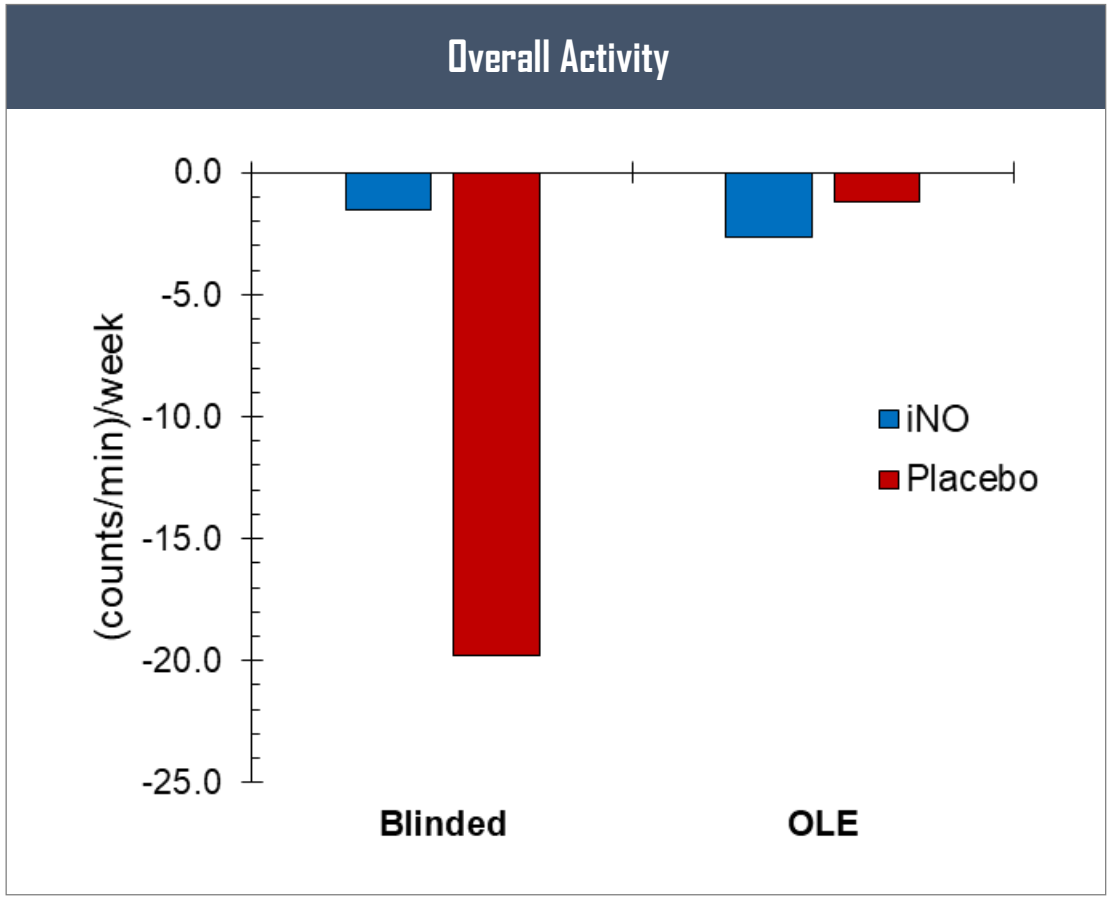
Benefit increases to 14 min/day (~20%) after 4 months of treatment

- p-value based on t-test on available data (exploratory endpoint; post-hoc analysis not adjusted for multiplicity)
- Data points and error bars = mean and standard error
- Month 2 analysis based on change from Week 1 to Week 8 and pooled placebo
- Month 4 analysis based on change from Month 1 to Month 4

Continued Benefit for Study Participants on Open Label Extension (OLE)

Study participants transitioning from placebo to active demonstrate trend reversal from deterioration to maintenance

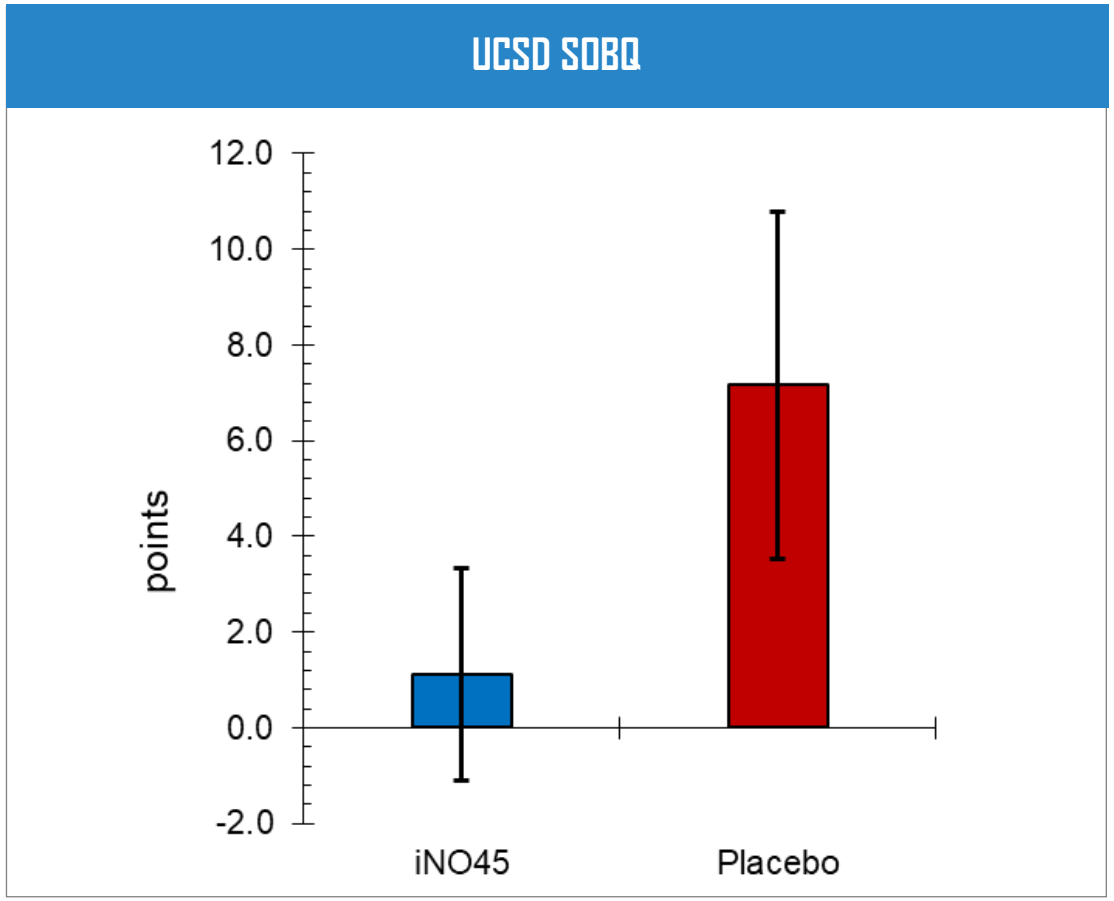




- MVPA = moderate to vigorous physical activity
- Change is based on Cohort I study participants with available data during blinded treatment and open label treatment (average 27 weeks of OLE) on all active doses

iNO45: UCSD Shortness of Breath Questionnaire (SOBQ) Indicates Benefit in Dyspnea

Increased score indicative of worsening



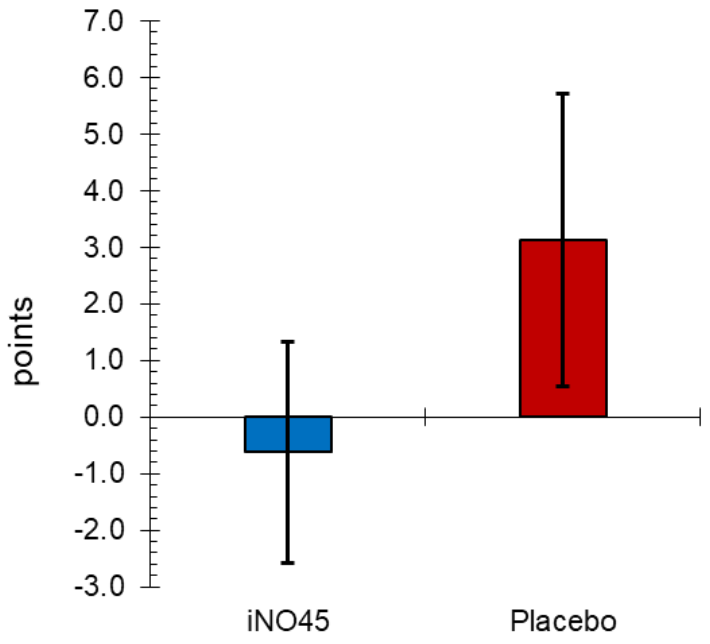
- Placebo corrected improvement of 4 points
- Measures shortness of breath while study participants perform daily physical activity

- Data points and error bars = LS Mean and Standard Error
- Longitudinal MMRM model includes baseline as covariate

iNO45: St. George's Respiratory Questionnaire (SGRQ) Indicates QOL Benefit in Multiple Measures

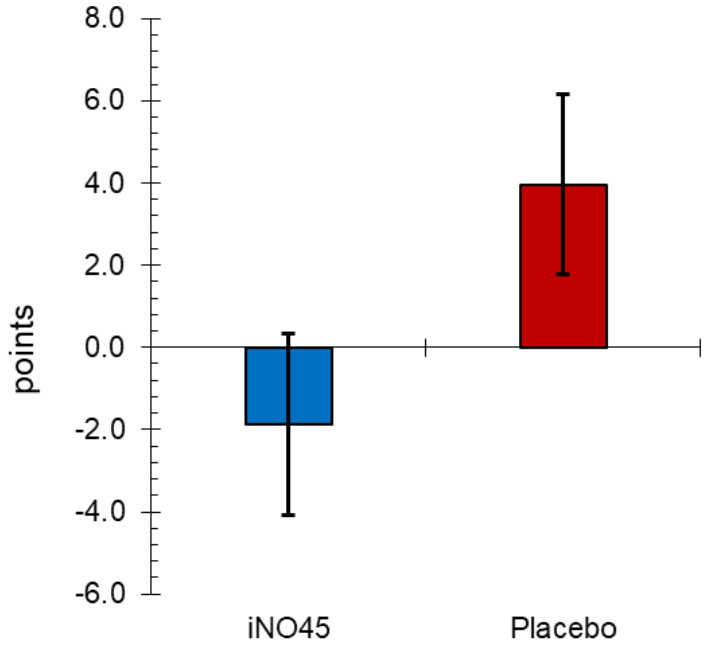
Increased score indicative of worsening

SGRQ Total



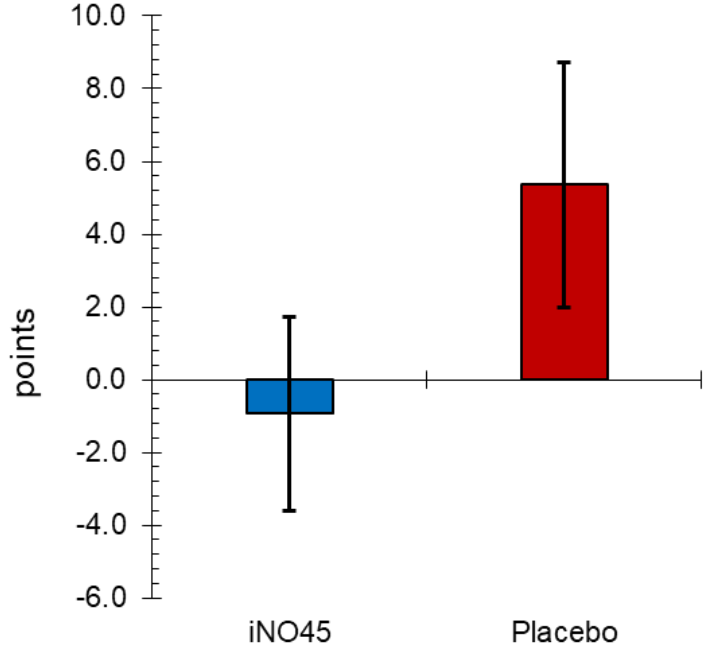
- Placebo corrected improvement of 4 points
- Measures health status and quality of life

SGRQ Activity



- Placebo corrected improvement of 6 points
- Measures disturbances to study participants' daily physical activity

SGRQ Impacts



- Placebo corrected improvement of 6 points
- Measures psychological and social impact of the disease

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- Data points and error bars = LS Mean and Standard Error
- Longitudinal MMRM model includes baseline as covariate

Phase 2 Safety Summary

INOpulse was well-tolerated in Cohort 1 and Cohort 2

- Incidence of SAEs was low in both active and placebo groups and all reported as unrelated to study drug
- AEs were balanced and generally non-serious with no observable trends

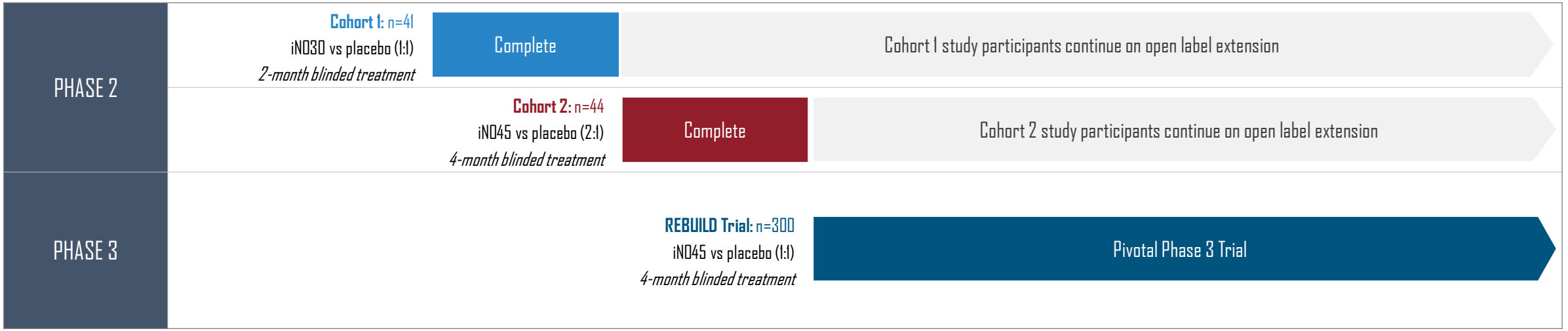
	Cohort 1 (8 weeks)		Cohort 2 (16 weeks)	
	iNO 30 n=23	Placebo n=18	iNO 45 n=30	Placebo n=14
Study participants with Adverse Events	19 (82.6%)	15 (83.3%)	26 (86.7%)	9 (64.3%)
Study participants with Serious Adverse Events	2 (8.7%)	2 (11.1%)	3 (10.0%)	3 (21.4%)
Total Serious Adverse Events Reported	3 (0.13/study participant)	4 (0.22/study participant)	4 (0.14/study participant)	7 (0.5/study participant)
Deaths	1 (4.3%)	0	0	0

Phase 2 Results Allow Immediate Transition into Pivotal Phase 3 Trial

FDA agreement on pivotal Phase 3 REBUILD study with MVPA as primary endpoint

Double-blind placebo-controlled study will assess study participants with fibrotic interstitial lung disease at risk of associated pulmonary hypertension

- Phase 2 Complete: Cohorts 1 and 2 suggest improvement in MVPA supported by other activity parameters and patient reported outcomes (Cohort 2)
- Phase 3: Pivotal REBUILD initiated with first patient enrolled in November 2020



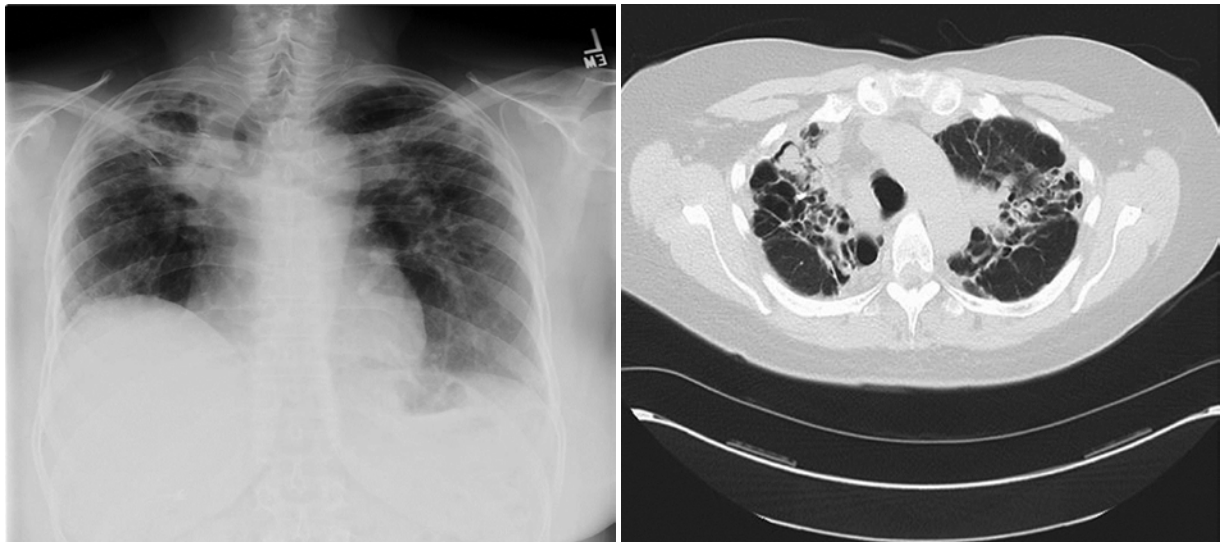
Pulmonary Hypertension associated with Sarcoidosis (PH-Sarc)

An Orphan Unmet Medical Need

Sarcoidosis is characterized by the growth of inflammatory cells (granulomas) most commonly in the lungs or lymphatic tissues

Prevalence of sarcoidosis is estimated at 200,000 in the US with up to 30% with associated pulmonary hypertension

Chest x-ray & CT of patient with PH-Sarc



Patients with associated PH have significantly reduced survival

	1-year survival	3-year survival	5-year survival
PH-Sarc	84%	74%	59%
Sarc	100%	96%	96%

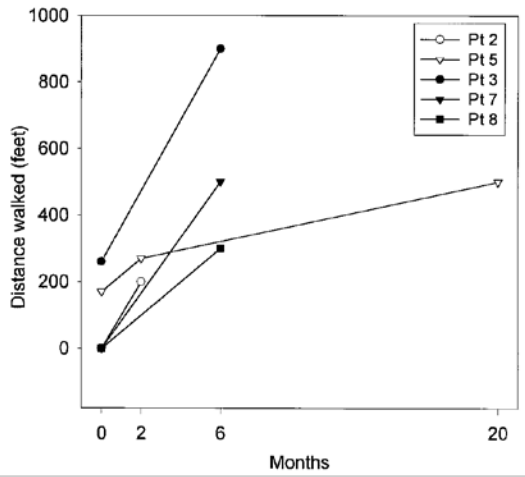
INOpulse MoA has the Potential to Provide Benefit to PH-Sarc Patients

Inhaled nitric oxide has been shown to improve hemodynamics and exercise capacity in PH-Sarc

Acute Hemodynamic Benefit on iNO

Parameter	% Change
mPAP	-18 ± 4
PVR	-31 ± 5
CO	12 ± 4

Chronic Benefit on Exercise Capacity



Systemic vasodilators exacerbate hypoxic vasoconstriction and cause hypoxemia

No approved therapy for treating PH in these patients

Phase 2 study designed to verify hemodynamic effect of INOpulse in PH-Sarc

- Acute dose escalation study with right heart catheterization
- Primary endpoint: change in mean PAP, PCWP, cardiac output and PVR
- Study results expected in 2021

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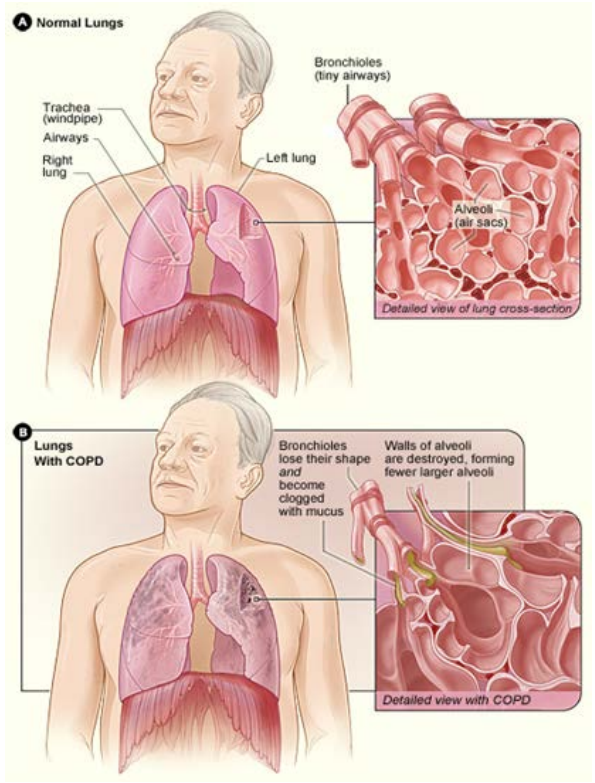
Preston et al., Chest, 2001

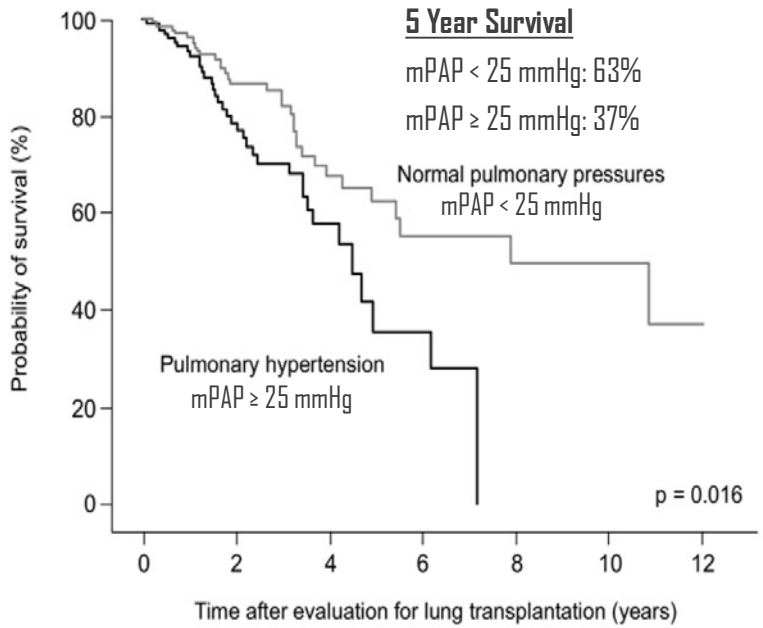
Pulmonary Hypertension associated with Chronic Obstructive Pulmonary Disease (PH-COPD) Represents Large Unmet Medical Need

COPD is a group of lung diseases characterized by progressive airflow obstruction and chronic airway inflammation



- Typically associated with smoking or exposure to other pollutants
- Obstruction of the bronchioles and alveoli reduces the ability to get oxygen and ultimately leads to hypoxemia
- Hypoxemia and inflammation contribute to development pulmonary hypertension

Pulmonary hypertension predicts survival in COPD



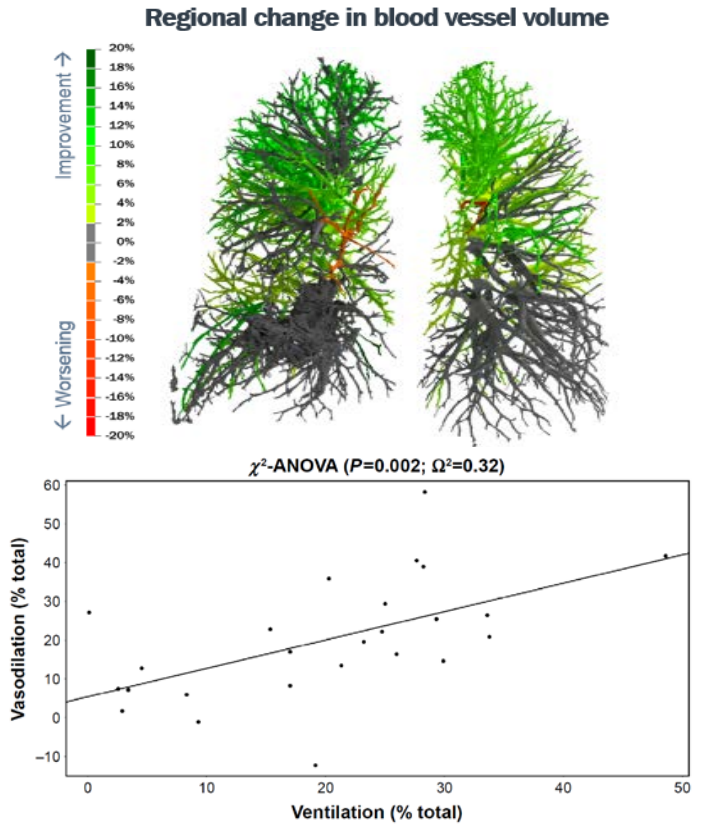
Survival years

No approved therapy for treating PH in these patients

Andersen KH et al. Prevalence, Predictors and Survival in Pulmonary Hypertension Related to End-stage Chronic Obstructive Pulmonary Disease. Journal of Heart and Lung Transplantation 2012; 31: 373-380.

INOpulse Provides Targeted Delivery and Improves Hemodynamics and Exercise Capacity in PH-COPD Patients

INOpulse targets delivery to well ventilated pulmonary vessels

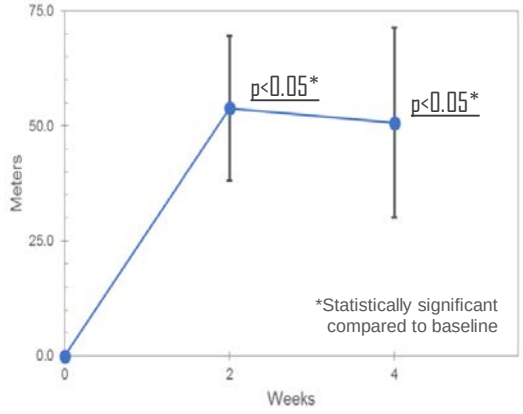


Chronic treatment with INOpulse provides statistically significant improvement in 6MWD and hemodynamics

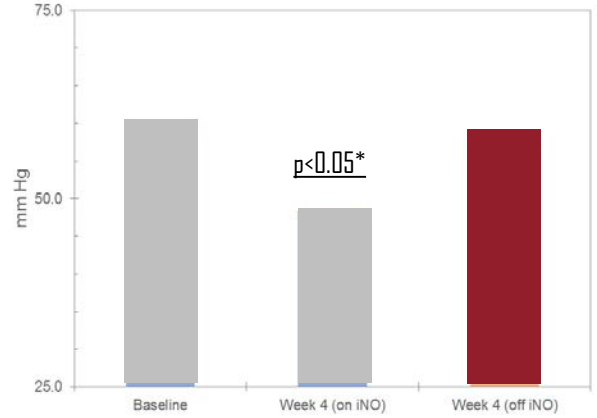
Study participants completing 4 weeks on iNO 30 demonstrated:

- Statistically significant increase in 6MWD at 2 weeks and 4 weeks (+50.7m)
- Statistically and clinically significant decrease in sPAP at 4 weeks (-12.0 mmHg; 19.9% reduction)
- sPAP increased to near baseline upon stopping treatment with iNO

Change in 6MWD



sPAP



Haijan et al., Int J of COPD, 2016

INOpulse Intellectual Property Protection

Patent	Status	Expiration	Description
Method of NO administration	US/EU: Issued Other Territories: Issued	Jan 2027	Covers consistent delivery of prescribed dose independent of respiratory rate
Breath Skipping & Pulse Volume Variation	US: Issued	Sept 2025	Covers skipping breaths or modifying pulse volume to ensure consistent dose independent of respiratory rate
Method of Administering High Concentration NO	US: Issued EU/Other Territories: Pending	Mar 2033	Limits delivery rate of high concentration iNO to prevent safety concerns
Optimized Pulse Shape	US: Issued	Jun 2039	Covers key parameters of pulse shape
INOpulse Design	US: Issued	Apr 2028	Covers design of the INOpulse device
Tip Purge	US/EU: Issued Other Territories: Pending	Apr 2033	Covers the use tip purge to ensure purity of iNO within the cannula
Triple-Lumen Cannula	US/ EU: Issued Other Territories: Pending	Dec 2033	Covers accurate dose delivery and reduced NO_2 formation
Index valve	US/EU: Issued Other Territories: Issued/Pending	May 2029	Ensures other cartridges cannot be used with INOpulse

Orphan Drug designation for IPF provides **exclusivity for 7 years (US) and up to 10 years (EU)**

Multiple pending and provisional patent applications filed from 2017-2020 that can **extend patent coverage into 2041**

Bellerophon THERAPEUTICS

Financial Summary

	Amount (in millions)
Cash and Cash Equivalents	$47.6[1]
Restricted Cash	$0.4[1]
Debt	$0[1]
Fully Diluted Shares Outstanding	12.2

1. As of December 31, 2020

Investment Highlights

Established iNO Therapeutic Benefit

- Approved for acute treatment of persistent pulmonary hypertension in neonates
- Positive results from multiple Phase 2 studies support INOpulse MoA and benefit

Advanced Clinical Stage Product

INOpulse technology focused on several large unmet orphan indications

fILD	PH-SARC / PH-COPD
Successful Phase 2 Proof of Concept studies in fILD	PH-Sarc: Phase 2 results expected in 2021
Positive Phase 2 results for Cohorts 1 and 2	PH-COPD: Successful Phase 2 study completed
Pivotal Phase 3 REBUILD study initiated in 4Q 2020 with FDA agreement on primary endpoint	PH-COPD: Phase 2b study design finalized in agreement w/ FDA

Proprietary INOpulse Technology

Strong IP protection on core programs up to 2039 and ability to extend coverage into 2041

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Bellerophon THERAPEUTICS