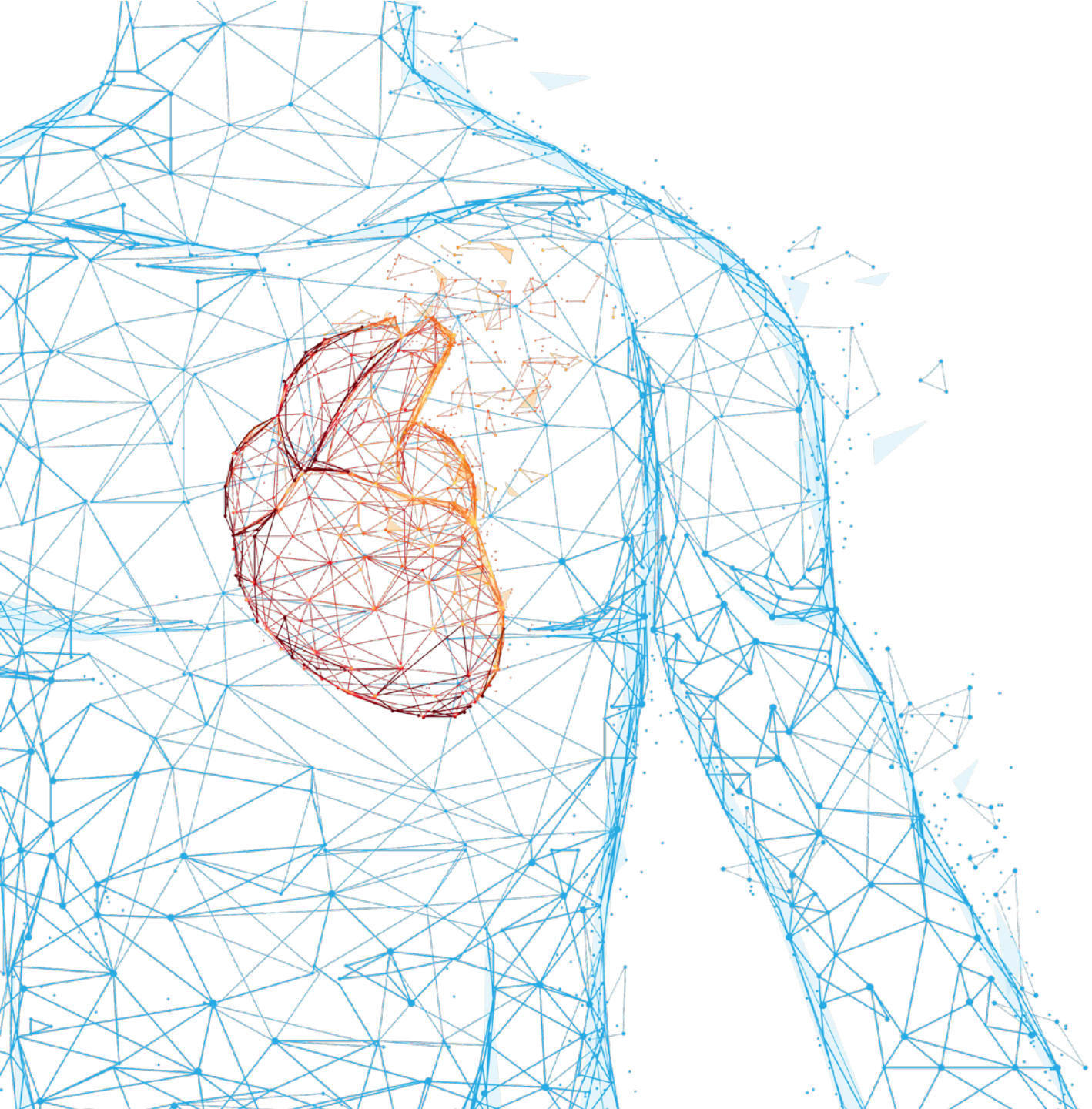


Bellerophon Therapeutics

Company Presentation I May 2023

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)

Late-stage biotherapeutics company developing inhaled nitric oxide (iNO) therapies to address significant unmet need in serious cardiopulmonary disorders

- **INOpulse® inhaled nitric oxide (iNO) for chronic use**
  - Targeted, pulsatile NO delivered via proprietary, portable, user-friendly device
  - Inhalational delivery to well ventilated areas of the lung overcomes drawbacks of systemic vasodilators
  - Positive results from multiple Phase 2 studies support mechanism of action
- **Broad market opportunity in multiple cardiopulmonary disorders**
  - Fibrotic interstitial lung disease (fILD) represents a broad underserved population >200K patients
  - Potential $1Bn+ markets in follow-on indications of pulmonary hypertension (PH) associated with sarcoidosis & chronic obstructive pulmonary disease (COPD)
  - IP protection up to 2039 before extensions
- **Simplified de-risked regulatory pathway**
  - NO approved for use in neonates (Ikaria); ability to leverage existing NDA
  - FDA agreement on MVPA primary endpoint in fILD Phase 3 REBUILD trial
- **Highly experienced leadership team and solid financials**
  - Unrestricted cash & equivalents $15.2 M[1]; no debt[1];
  - 13.8 M fully diluted shares outstanding [2]

1. As of March 31, 2023
2. Represents outstanding shares, options, RSU's and warrants as of March 31, 2023

Highly Experienced Leadership Team with Expertise in Respiratory, Rare Diseases & Medical Devices

Peter Fernandes
Chief Executive Officer

Parag Shah, Ph.D.
VP, Business Operations

Bobae Kim
VP, Regulatory Affairs & Quality Assurance

Martin Dekker
VP, Device Engineering & Manufacturing

Manfred Hanuschek
Financial Consultant

Ashika Ahmed, MBBS
Director Drug & Device Safety Physician

Addressing Unmet Needs in Multiple Cardiopulmonary Diseases

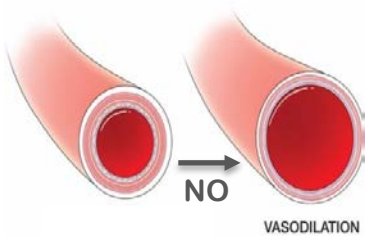
INOpulse development pipeline

Indication	Phase 1	Phase 2	Phase 3	Current Status
fILD Fibrotic Interstitial Lung Disease at risk of Pulmonary Hypertension				**REBUILD trial recruiting** Underpinned by positive Phase 2 acute hemodynamic trial (2020) & Phase 2 chronic trial (2019)
PH-SARC Pulmonary Hypertension associated with Sarcoidosis				**Acute hemodynamic study completed** Positive study results reported end-2021 Phase 2 chronic use trial designed and cleared by FDA
PH-COPD Pulmonary Hypertension associated with COPD				**Phase 2b ready** Multiple phase 2 studies completed Phase 2b trial design finalized

Nitric Oxide is a well-established vasodilator being developed for ambulatory setting

Portable Delivery System Allows Chronic iNO Therapy

Nitric Oxide



"Molecule of the Year" 1992[1]

Nobel Prize for discovering its signaling role[2]

BELLEROPHON: Ambulatory chronic therapy

INOpulse®

- Portable pulsatile iNO delivery system for use in chronic in-home setting
- 447 patients treated to date in PH trials; average duration of ~10 months each
- Additional 368 patients treated as part of COVID-19 related clinical trial
- Cumulative subject exposure 350+ years; longest subject treatment 8+ years[3]

Mallinckrodt: Hospital based acute therapy

- Approved for use in 1999 for persistent pulmonary hypertension in neonates
- Continuous flow iNO delivery system for acute administration
- Commercially established for 20+ years

Bellerophon THERAPEUTICS

1. SoRelle, R.; Circulation, 1998, 2365-2366; 2. Furchgott, Ignarro, Murad 1998 Nobel Prize in Physiology or Medicine 1998; 3. Subject was enrolled in PAH201 study in 2012 and transitioned to INOpulse Delivery System in 2016.

INOpulse is a Proprietary Drug-Device Combination Therapy

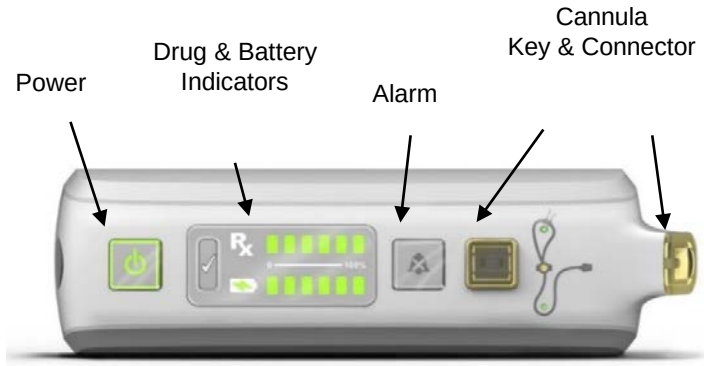
Broad IP portfolio around drug cartridge, delivery device and tri-lumen cannula

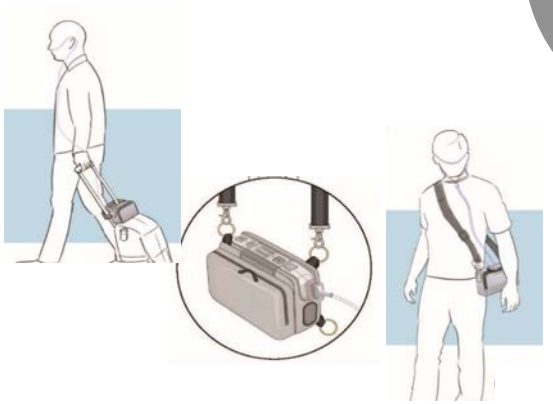
01 Intuitive and easy to use device delivers pulsed doses of nitric oxide to the patient

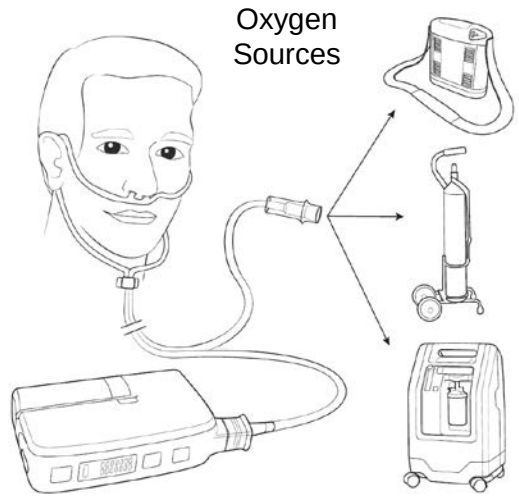
02 Drug cartridge engages with device via a simple swing mechanism

03 Novel tri-lumen cannula allows concomitant delivery of nitric oxide and oxygen therapy

04 Lightweight portable design allows ease of transport for home use by ambulatory patients







Preventing Ventilation/Perfusion Mismatch is Critical in PH

Baseline

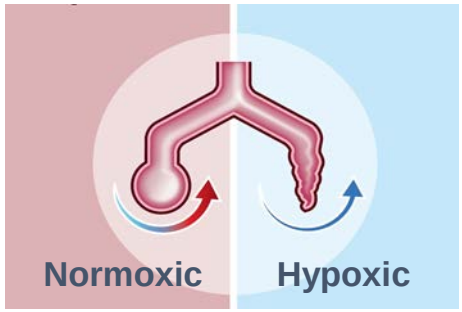
Significant lung disease results in alveolar hypoxia

⌄⌄

Triggers protective hypoxic vasoconstriction response

⌄⌄

Prevents systemic oxygen desaturation but increases pulmonary pressure resulting in PH

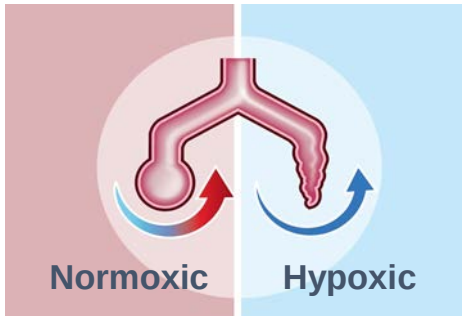


Systemic therapies

Generalized vasodilation

Reverses protective hypoxic vasoconstriction response

Results in ventilation / perfusion (V/Q) mismatch and worsened systemic oxygenation



INOpulse®

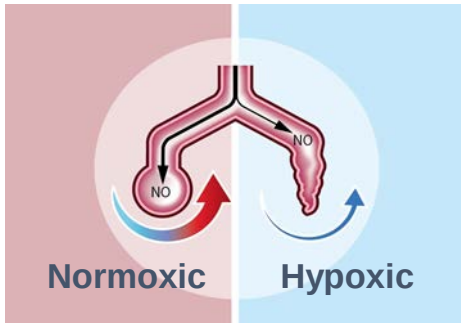
Targeted vasodilation of only well ventilated alveoli

⌄⌄

Synergistic with hypoxic vasoconstriction response

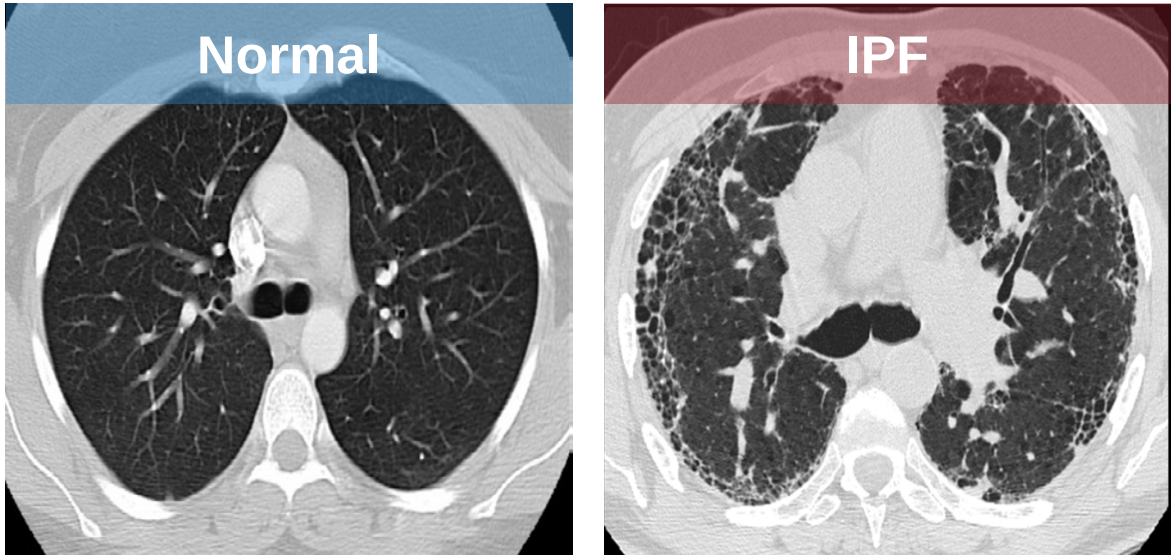
⌄⌄

Prevents V/Q mismatch, improves systemic oxygenation, improves PH



Fibrotic Interstitial Lung Disease (fILD)

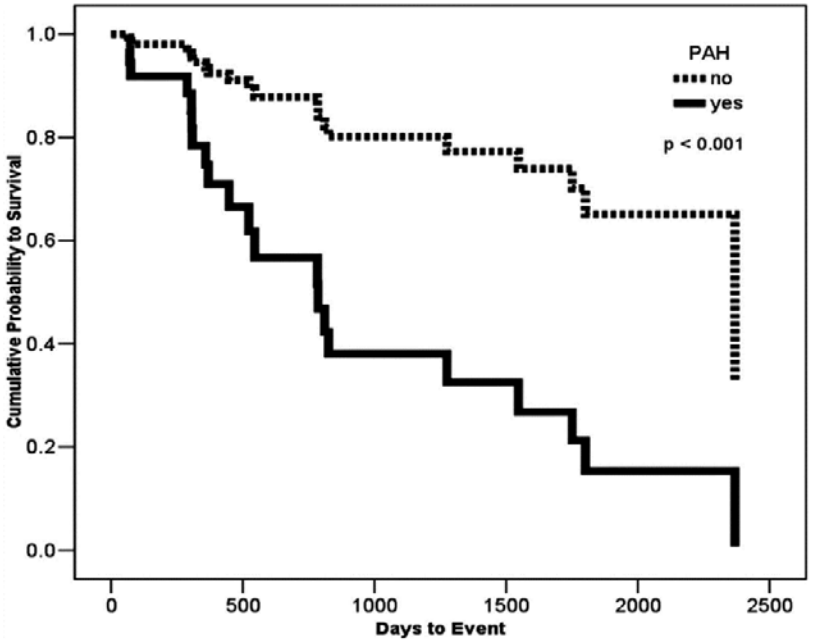
A broad category of diffuse lung diseases with significant unmet need



- Characterized by variable amounts of inflammation and fibrosis of lung air sacs
- Idiopathic Pulmonary Fibrosis (IPF) is the most commonly diagnosed and most serious fILD
- Patients often require supplemental oxygen (O_2) to maintain O_2 saturation
- Severely impaired quality of life and limitations on activities of daily living
- Prognosis and survival significantly worse for patients with associated pulmonary hypertension (PH)

Pulmonary Hypertension (PH) associated with fILD Significantly Reduces Survival

Pulmonary Hypertension as Predictor of Survival in IPF



~40% of IPF patients exhibit PH symptoms at rest

3x increase in risk of death with PH-IPF vs. IPF alone

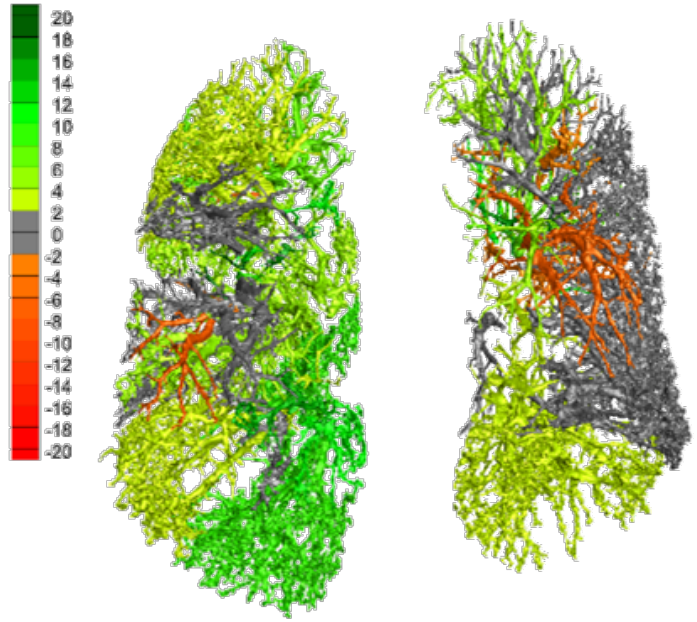
0 approved therapies to improve physical function or quality of life†

Rivera-Lebron, Advances in Pulmonary Hypertension, 2013, 12:127-134; † Tyvaso (inhaled Treprostinil) recently approved to improve 6MWD in PH-ILD

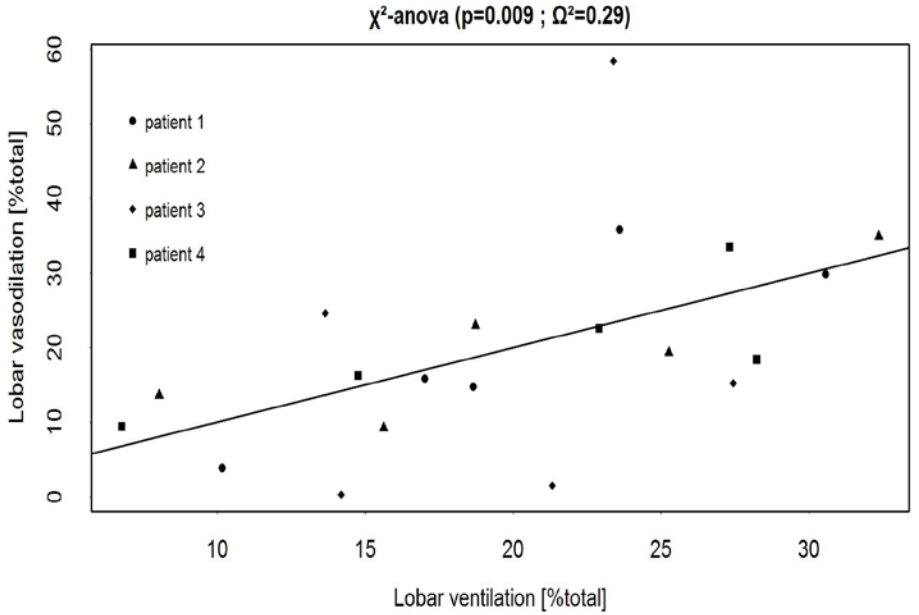
INOpulse Demonstrates Targeted Vasodilation in fILD Supporting the Mechanism of Action

Acute Phase 2 Data Showed Immediate Benefit of INOpulse on Vasodilation and Ventilation/Perfusion Matching

Targeted vasodilation to better ventilated areas of lung



Significant correlation between ventilation/vasodilation matching



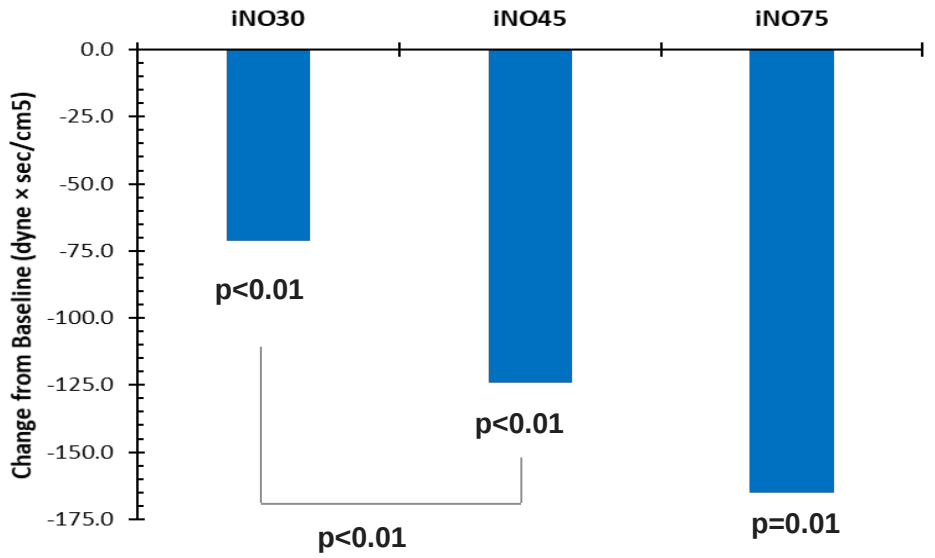
Haijan et al., ATS 2017, Poster Presentation

Acute Hemodynamic Benefit in fILD Supports Continuing iNO45 in Phase 2b/3

Clinically and statistically meaningful cardiopulmonary improvement on iNO30 with statistically significant benefit in PVR on dose escalation to iNO45

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

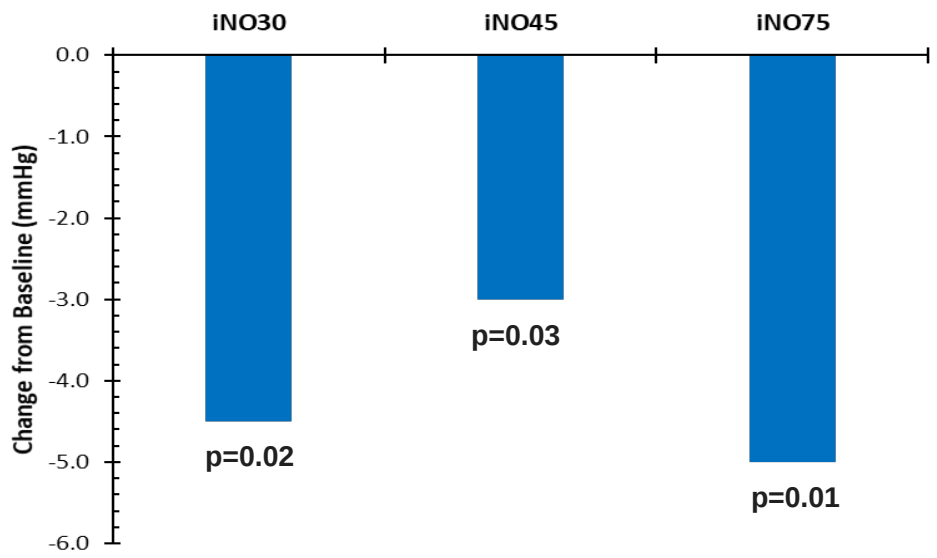
Pulmonary Vascular Resistance (PVR)



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

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

Phase 2 Development in fILD used to Select Primary Endpoint

Exploratory trial designed to identify optimal endpoints and dose for Phase 3 trial

PHASE 2 Chronic study	**Cohort 1: n=41** iNO30 vs placebo (1:1) *2-month blinded treatment*	Complete → Cohort 1 study participants continue in open label extension (OLE)
	Cohort 2: n=44 iNO45 vs placebo (2:1) *4-month blinded treatment*	Complete → Cohort 2 study participants continue in open label extension (OLE)

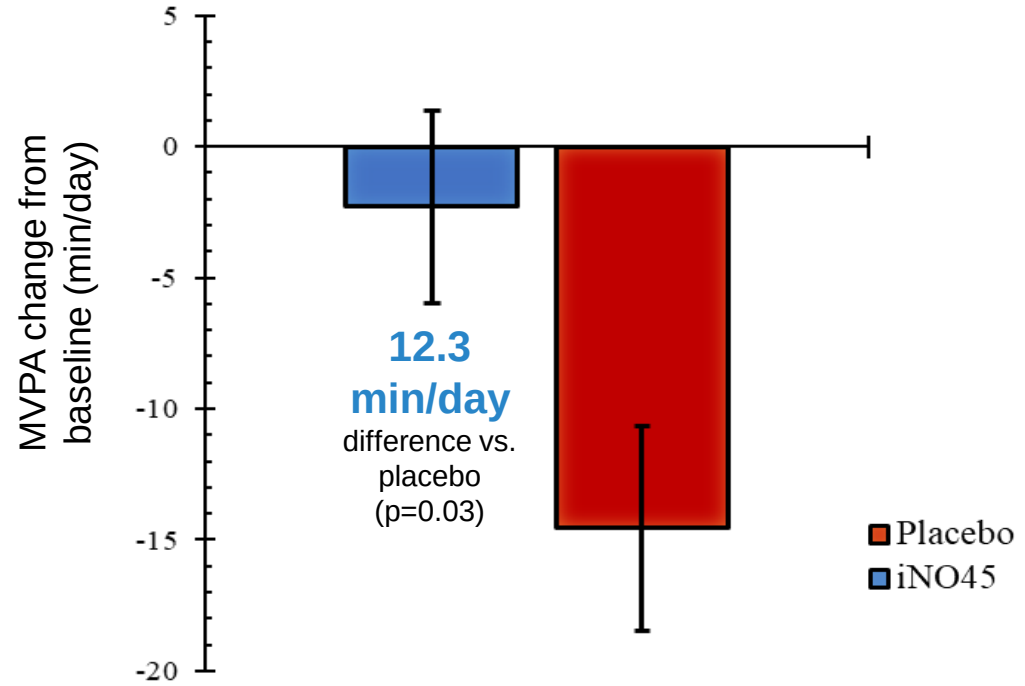
- Trial assessed multiple exploratory endpoints including actigraphy (continuous monitoring of daily physical activity) and patient reported outcomes
- Both cohorts supported use of MVPA (moderate to vigorous physical activity) assessed by actigraphy as the optimal endpoint to progress into Phase 3
- FDA acceptance of the overall study design and MVPA as the primary endpoint for the Phase 3 registration study, with the validation of the MVPA endpoint by establishing meaningful changes in in PROs

fILD diagnosed in accordance with accepted guidelines and confirmed by high resolution CT (HRCT) scan; Forced vital capacity (FVC) of ≥ 40% predicted in the 6 months prior to screening; Needing supplemental oxygen defined as desaturation to ≤ 88% at rest or with exertion

Phase 2 data supports use of MVPA measurement as primary endpoint for Phase 3 trial

Target patient population has a median survival of 1.5 to 2 years and typically struggle to perform basic activities such as walking up stairs, showering, housework†

Moderate to vigorous physical activity (MVPA; min/day) maintained on iNO45 while placebo patients deteriorate



MMRM analysis based on change from Month 1 to Month 4; data points and error bars = LS mean and standard error; p-value not adjusted for multiplicity

14.6 min/day decline in MVPA on placebo; 2.3 min/day decline in MVPA on iNO45 at month 4

- 12.3 min/day (~21%) difference in time spent in MVPA as compared to placebo
- 10-20% change in actigraphy parameters estimated to be clinically relevant in diseased populations (fILD, COPD, heart failure)‡

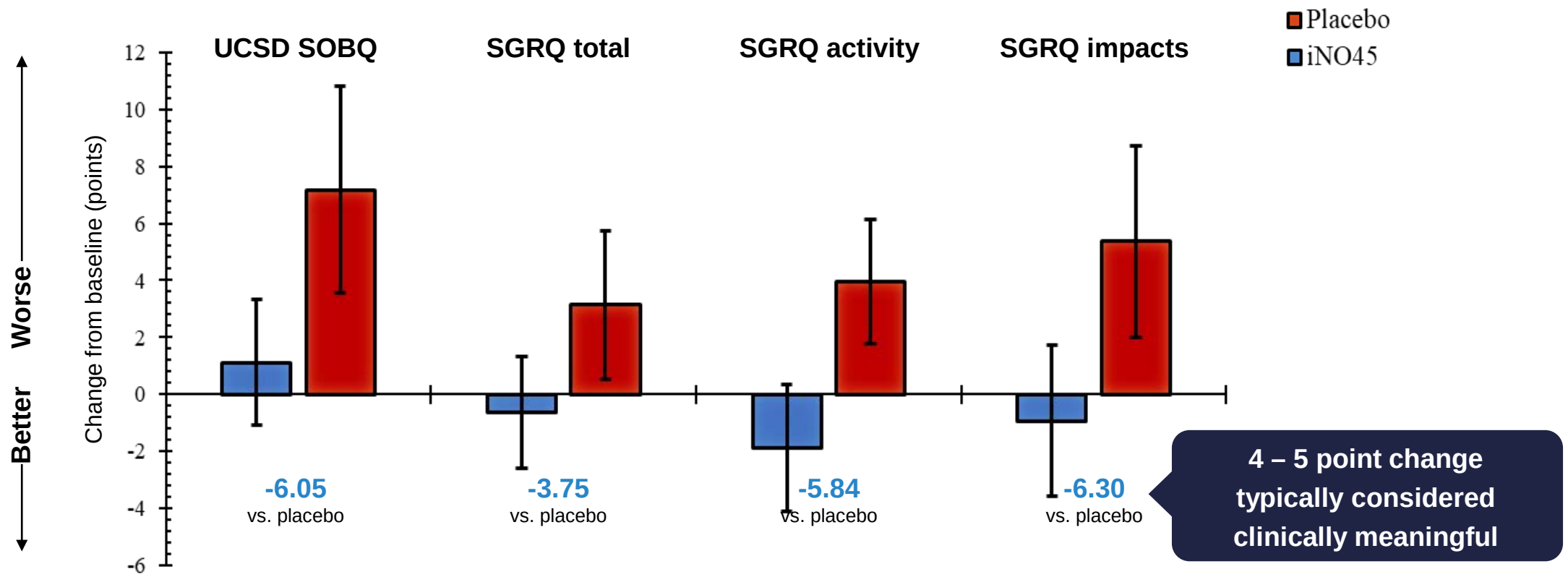
Similar trend seen in overall activity

- iNO45 group remained stable
- ~6% placebo adjusted difference (89.4 counts/min)

King *et al*., Annals of American Thoracic Society, 2022, 19, 4, 594-602, https://doi.org/10.1513/AnnalsATS.202107-864OC; †. Rivera-Lebron, Advances in Pulmonary Hypertension, 2013, 12:127-134; "IPF Voice of Patient", FDA Meeting and Report, 2015; ‡ Hur, et al, 2019; Teylan et al., Chron Respir Dis., 2019, 16:1479973118816424; Demeyer et al., PLoS One. 2016;11:e0154587; Shoemaker MJ, World Journal of Cardiovascular Diseases; 2012., 129-35

MVPA Results Mirrored Closely by Patient Reported Outcomes

Outcomes measured by UCSD Shortness Of Breath Questionnaire (SOBQ) and St. George's Respiratory Questionnaire (SGRQ) remained stable on iNO45 vs. deterioration on placebo



MMRM analysis based on change from Baseline to Month 4; data points and error bars = LS mean and standard error

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
Patients with Adverse Events	19 (82.6%)	15 (83.3%)	26 (86.7%)	9 (64.3%)
Patients with Serious Adverse Events	2 (8.7%)	2 (11.1%)	3 (10.0%)	3 (21.4%)
Total Serious Adverse Events Reported	3 (0.13/patient)	4 (0.22/patient)	4 (0.14/patient)	7 (0.5/patient)
Deaths	1 (4.3%)	0	0	0

Phase 2 fILD Key Takeaways

Data supported move to Phase 3 with MVPA as a primary endpoint

Observed meaningful effects on key activity levels and patient reported outcomes (PRO)

- INOpulse (iNO30 and iNO45) group maintain activity levels while placebo group deteriorates across activity parameters
- iNO45 group maintain PRO scores (UCSD & SGRQ) while placebo group deteriorates consistent with change in activity levels
- Physical activity levels maintained during OLE; patients switching from placebo to active demonstrated reversal in decline

Generally well-tolerated with no serious adverse events considered related to INOpulse

INOpulse®

Advanced into Phase 3 REBUILD study in fILD

Analysis of Phase 2 & Phase 3 Data Supported Reducing Trial Size to 140 Patients

Prior trial size of 300 patients was overpowered to achieve a p-value <0.01

FDA and DMC (Data Monitoring Committee) accepted reduction in trial size based on statistical and safety assessment

Attribute	Considerations
Primary Endpoint: MVPA	• MVPA is >90% powered for p=0.01 and p=0.05 at 140 total patients • Analysis conducted by independent statistical consultant on Phase 2 data utilizing analysis methodology to be used in Phase 3 REBUILD trial
REBUILD MVPA Baseline	• Comparable MVPA baseline characteristics between Phase 2 and REBUILD supports similar patient characteristics and population
Safety Analysis	• Independent Data Monitoring Committee indicated that review of first 85 Phase 3 patients shows no safety concern with regards to reduction of REBUILD study size to 140 patients

Regulatory Feedback	• FDA verified ***No Objection*** to proposed reduction in sample size to 140 patients
	  • Assessment based on review of statistical analysis of Phase 2 data, baseline MVPA comparison between Phase 2 and Phase 3, and DMC review of safety data in Phase 3
	  • FDA noted that sample size reduction may further limit the acquisition of information on other, important clinical endpoints in the trial.

Cohort 2 Evaluated Utilizing Phase 3 REBUILD Analysis Methodology as Agreed with FDA

Primary endpoint is >90% powered at 140 patients for p<0.01

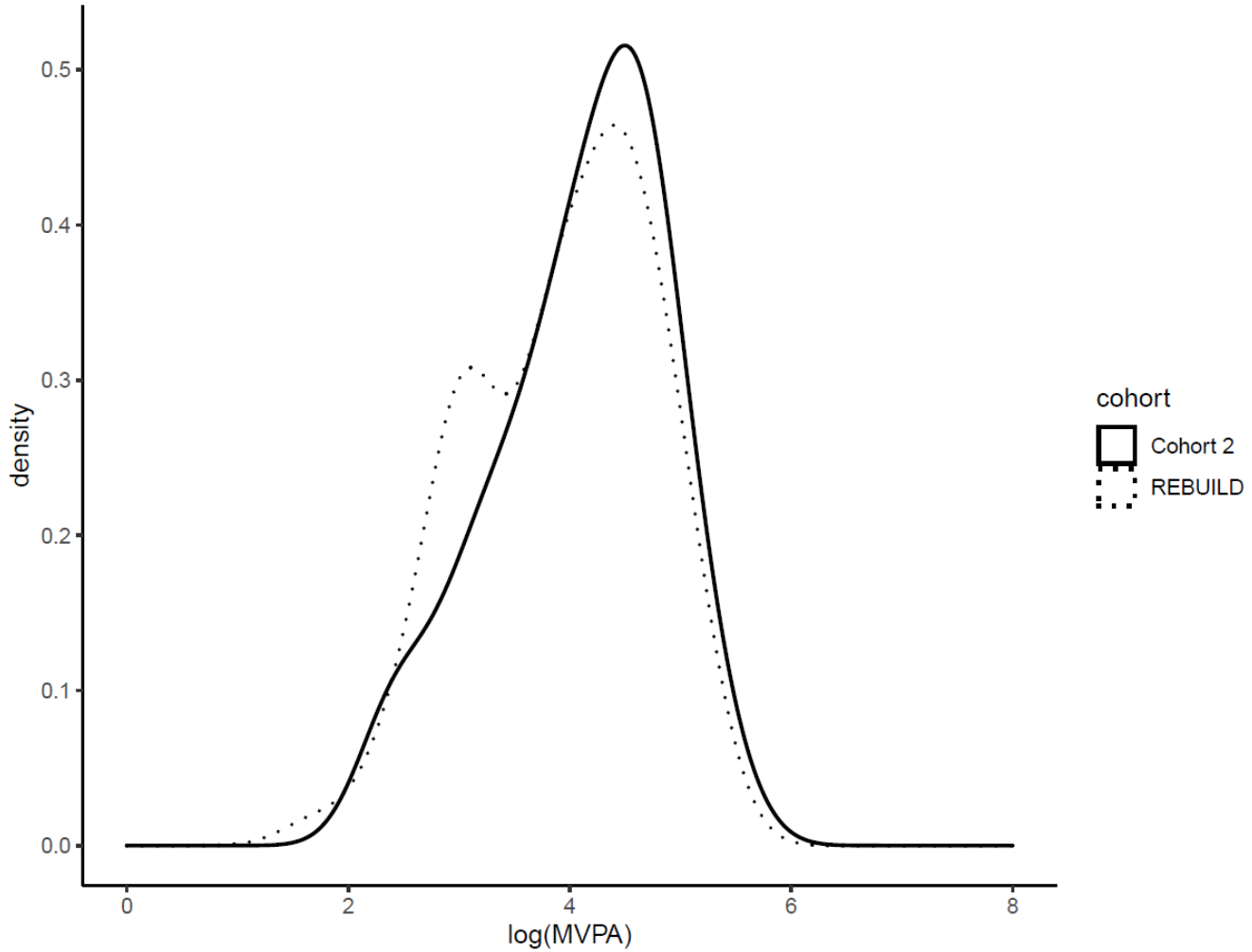
Endpoint	Significance Level	Cohort 2 Estimate of treatment effect	Sample size for 90% power	Revised Trial Size *N=140 patients N=70/arm*	Prior Trial Size *N=300 patients N=150/arm*	Data Analysis
MVPA (REBUILD Primary endpoint)	0.05	0.735 SD=1	N=80	99%	99%	• Cohort 2 bi-weekly actigraphy • Criteria Bi-Week 4 (weeks 7-16)
	0.01		N=114	95%	99%	

Phase 3 REBUILD Analysis Methodology:

- MVPA will be assessed via actigraphy using bi-weekly (14 day) periods with baseline measured prior to randomization
  - Compliant bi-week is defined as minimum of 8 compliant days of which at least 2 are weekend days
  - Compliant day is defined as at least 600 minutes of wear-awake time within the day
- Analysis is based on MMRM change in log-transformed MVPA during the second half of blinded treatment (bi-weeks 4 to 8)
- Cohort 2 treatment effect of 0.735 (effect size ÷ standard deviation) was used to determine powering estimate for Phase 3 REBUILD

Similar Baseline MVPA Distribution Between Cohort 2 & REBUILD

REBUILD analysis based on blinded assessment of first 80 randomized patients

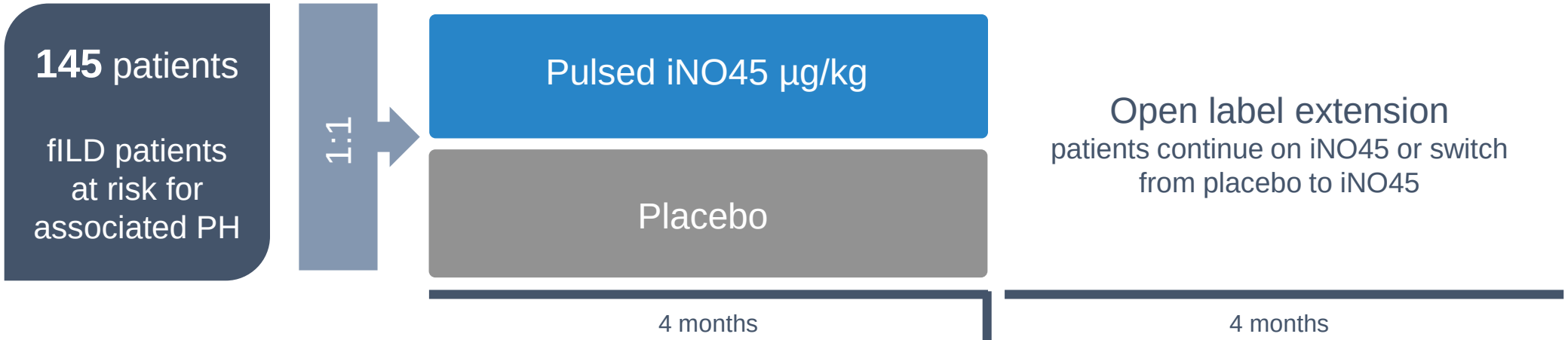


Consultant Report, Sample Size Considerations for PULSE-PHPF-001 (REBUILD study), July 20, 2022

Pivotal Phase 3 Trial in fILD

REBUILD

FDA acceptance on study size and design with MVPA as the primary endpoint
Enrollment completed earlier than expected in January 2023 with top-line results in mid 2023



✓ FDA acceptance of the overall study design and MVPA as the primary endpoint for the Phase 3 registration study, with the validation of the MVPA endpoint established by its confirmation vs. PROs

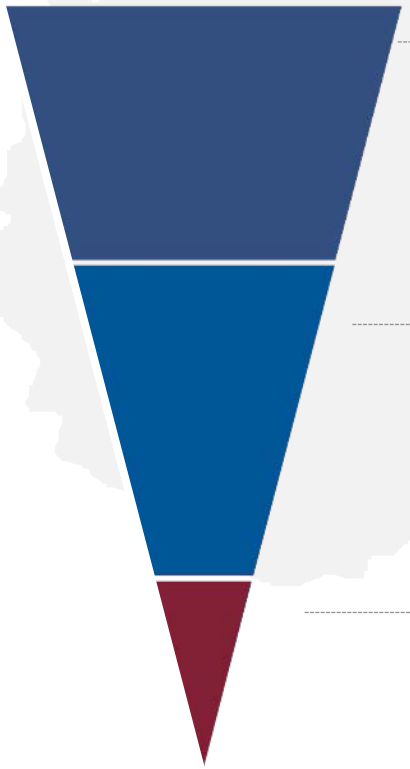
Primary Endpoint

- Change in MVPA assessed by Actigraphy
- Safety

Additional Endpoints

- Change in Overall Activity assessed by Actigraphy
- Patient Reported Outcomes (SGRQ, UCSD, PROMIS® SF, PGIS/C)
- Time to Clinical Worsening

fILD Represents a Significant Market Opportunity in the US and Beyond



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%

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

Source: LEK INOpulse Market Research Report (2018); addressable population includes PH-ILD, with the majority on LTOT (long-term oxygen therapy); physician adoption rate based on product profile prior to identifying MVPA as the primary endpoint in REBUILD Phase 3 trial

INOpulse Could Address Multiple Large Market Opportunities

	Significant Unmet Need		Large Potential Market	
fILD (fibrotic interstitial lung disease at risk of pulmonary hypertension)	fILD with PH reduces 1-year survival from 28% to 5.5%[5]	1 approved therapy; no approved therapy to improve physical function or quality of life	226,000 fILD in the US; 30-40% with associated PH[4]	$2B+ market opportunity
PH-SARC (sarcoidosis associated with pulmonary hypertension)	SARC with PH reduces 5-year survival from 96% to 59% [1]	0 approved therapies	200,000 Sarc prevalence in the US; up to 30% with associated PH[2]	$1B+ market opportunity
PH-COPD (COPD associated with pulmonary hypertension)	COPD with PH reduces 5-year survival from 63% to 37%[3]	0 approved therapies	12.7 M diagnosed COPD in the U.S; ~27% with associated PH[4]	Multi-billion $ market opportunity

1. Huitema et al., Neth Heart J, 2016, 24:390–399; Nunes et al., Thorax, 2006, 61:68–74; 2. Baughman et al., Annals ATS, 2016, 13:1244-1252; 3. Andersen KH et al. J Heart Lung Trans, 2012; 31:373-380; Oswald-Mammosser et al., Chest, 1995, 107:1193-1198; 4. LEK INOpulse Market Research Report (2018); 5. Rivera-Lebron, Advances in Pulmonary Hypertension, 2013, 12:127-134

Beyond fILD: Positive top-line Phase 2 data in PH-Sarcoidosis

Dose-escalation study designed to verify acute hemodynamic effect of INOpulse

All 8 patients demonstrated decreases in mPAP and PVR across the doses of INOpulse utilized in the study

- iNO45 dose median decrease of 20% (-54% to +22%) in PVR, compared to a median baseline PVR of 329 dyne×cm×sec-5
- iNO125 dose (7 out of 8 patients) median decrease of 29% (-43% to -5%) in PVR p=0.02 vs. baseline and prior dose)
- mPAP decreased by a median of 6-10% across the doses of iNO30 to iNO125, compared to median baseline of 37.2 mmHg

Generally well-tolerated

- No treatment-emergent adverse events or serious adverse events

Acute hemodynamic data supports progressing to a chronic dosing Phase 2b study

✓ **20%+** reduction in PVR which is typically considered clinically meaningful

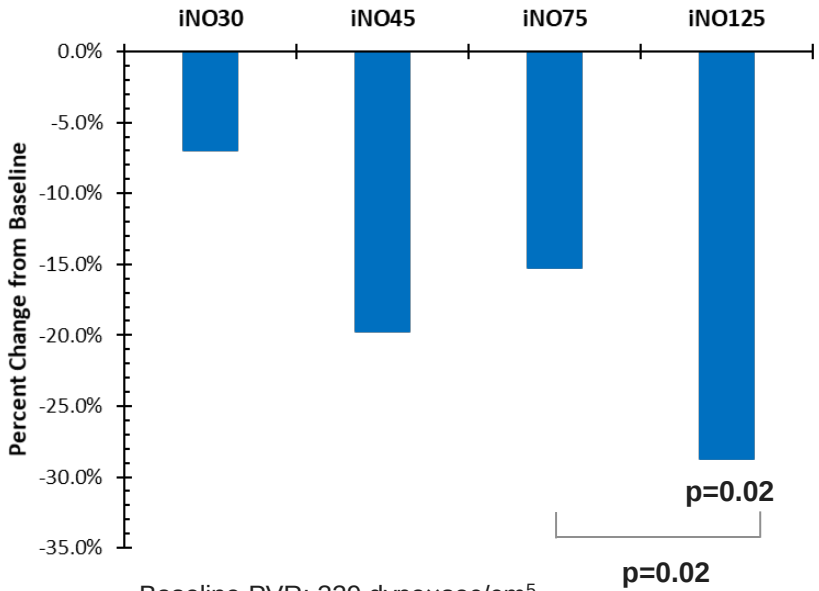
Current Status: Exploratory Phase 2 chronic use trial to assess safety & efficacy cleared by FDA

mPAP – mean pulmonary arterial pressure; PVR – pulmonary vascular resistance; p-value based on Wilcoxon Rank Test (no correction for multiplicity); range represents max and min values for each condition; data based on 8 PH-Sarc patients; 7 of 8 patients escalated to dose of iNO125

INOpulse Demonstrates Acute Hemodynamic Improvement in PH-Sarc

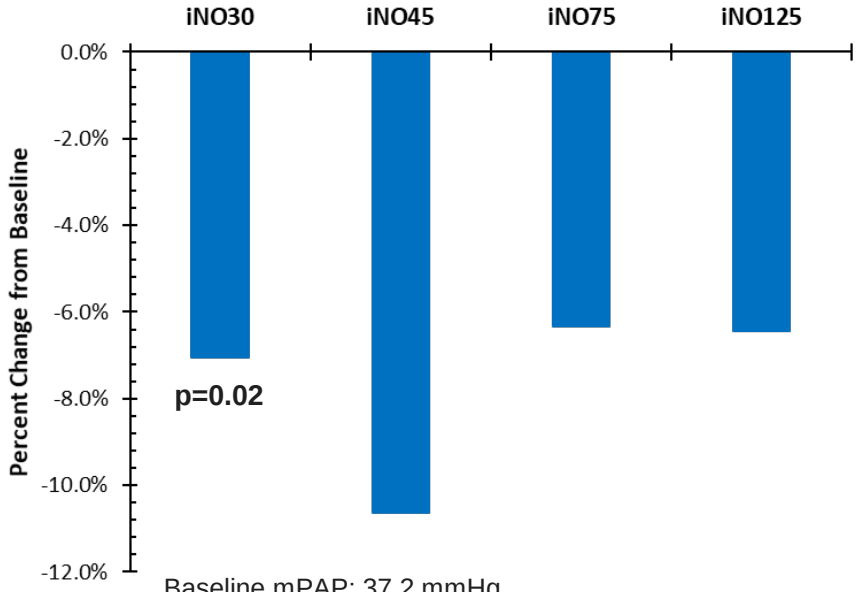
- Pulmonary hemodynamics measured via right heart catheterization at baseline and following each sequential iNO dose
- Clinically meaningful reduction in PVR on iNO45 with potentially increased benefit at highest dose of iNO125
- No treatment-emergent adverse events (TEAEs) or serious adverse events (TESAEs)

Pulmonary Vascular Resistance (PVR)



Baseline PVR: 329 dyne×sec/cm^5

mean Pulmonary Arterial Pressure (mPAP)

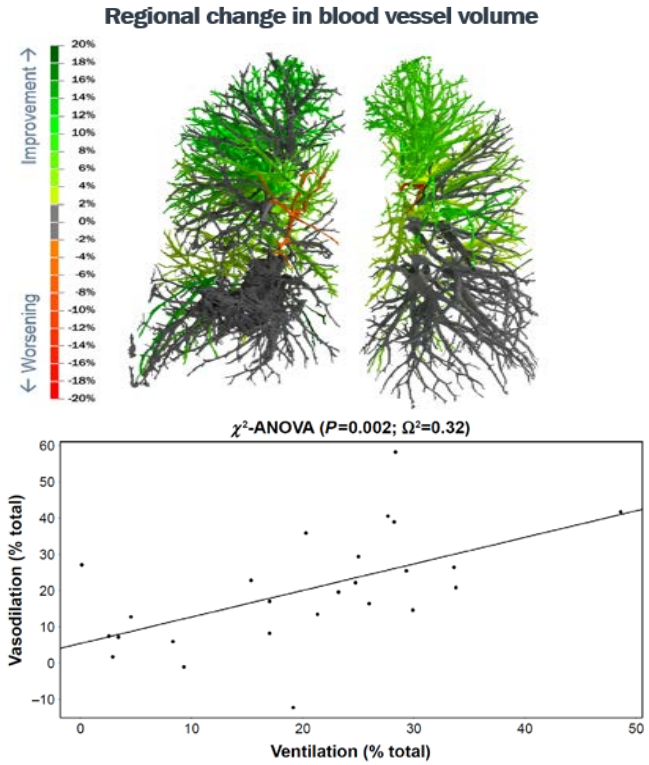


Baseline mPAP: 37.2 mmHg

Baseline values are median of the group; bar graphs are median values at each assessment for all available study participants; p-value based on Wilcoxon Rank Test between baseline and each dose and between dose and prior dose (no correction for multiplicity); Data based on 8 PH-Sarc patients; 7 of 8 patients escalated to dose of iNO125

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

Delivery to well ventilated pulmonary vessels and ventilation/vasodilation matching



Patients completing 4 weeks of chronic treatment on iNO30 demonstrated:

- Statistically significant increase in 6MWD at 2 weeks and 4 weeks (+50.7m) as compared to baseline
- 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
- The iNO therapy was well tolerated with no related safety concerns

Primary concepts for Phase 2b trial design in agreement with FDA

Haijan et al., Int J of COPD, 2016

Compelling Investment Opportunity in Late Stage Biotherapeutics Company with Multiple High Value Indications

Clinically validated approach

- NO is a proven, well-established vasodilator approved for acute use in persistent pulmonary hypertension in neonates
- Being developed for chronic administration to address multiple significant unmet and underserved needs

Clear development pathway

- Phase 2a completed establishing V/Q matching and acute hemodynamics
- Phase 3 ongoing for lead program in fILD; PH-Sarc and PH-COPD are Phase 2b ready
- Simplified, de-risked approval pathway with ability to leverage Ikaria's existing NDA

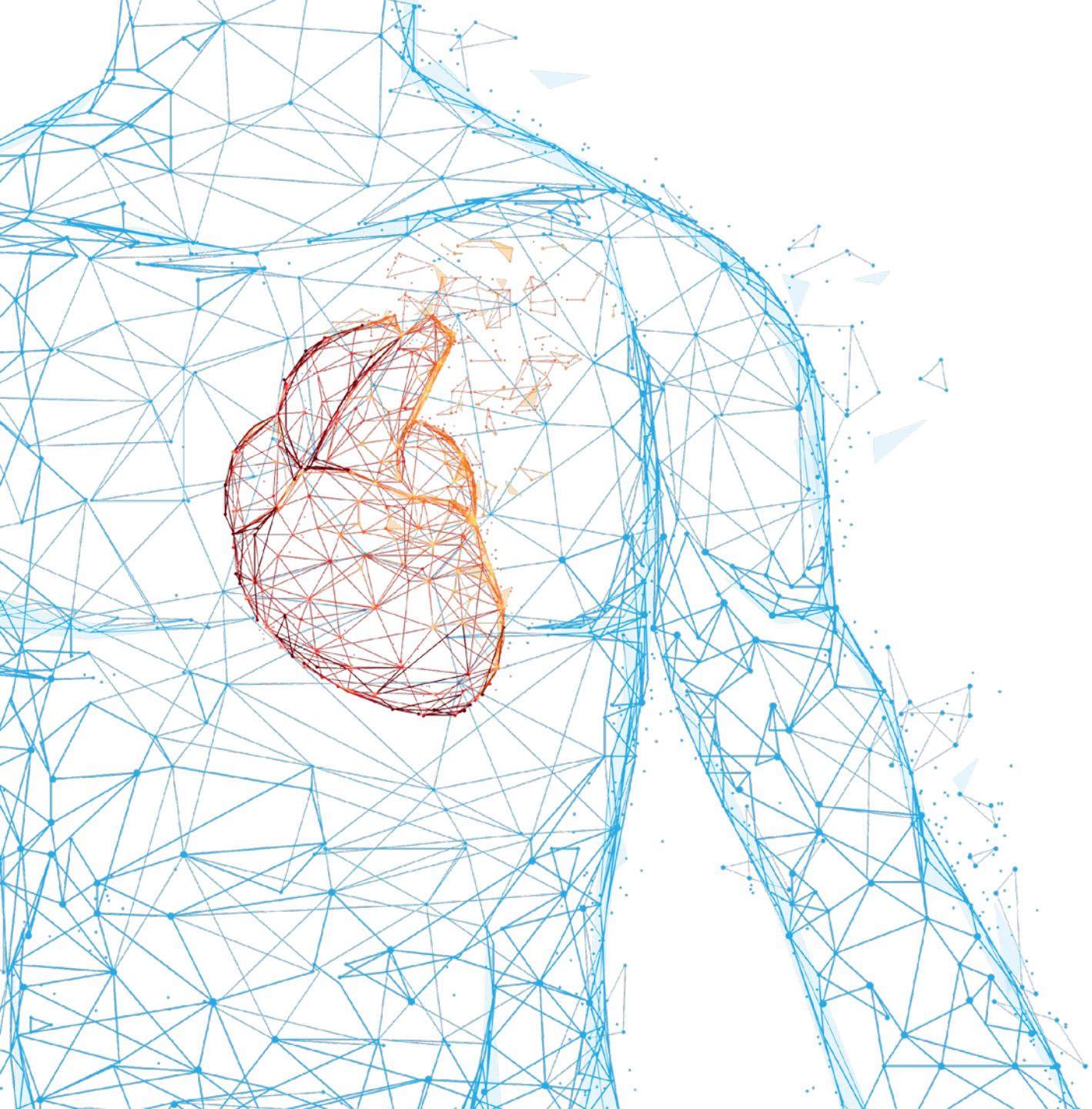
Large market opportunities

- Targeting $2Bn+ market in fILD
- Potential $1Bn+ markets in follow-on indications of PH-Sarc and PH-COPD
- IP protection through 2039

Corporate profile

- Highly experienced team with expertise in rare and respiratory disease
- Unrestricted cash & equivalents of $15.2 M[1], no debt
- 13.8 M fully diluted shares outstanding[2]

1. As of March 31, 2023
2. Represents outstanding shares, options, RSU's and warrants as of March 31, 2023



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