# Bellerophon Therapeutics

Company Presentation I May 2019

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: 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)

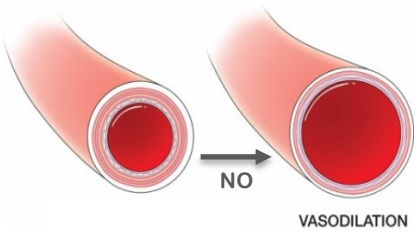
## Company Profile

| | |
|---|---|
| Clinical-Stage Biotherapeutics Company | • Company spun-off from Ikaria<br>• Focused on developing inhaled nitric oxide (iNO) based therapies for outpatient management of chronic pulmonary diseases<br>• Portable, lightweight delivery system allows for chronic home use |
| Novel Therapy Addressing Unmet Medical Needs | • Ongoing PH-ILD study modified to seamless Phase 2/3 based on positive results for first cohort and recent agreement with FDA<br>• PH-COPD Phase 2b study design finalized with FDA<br>• PH-Sarc Phase 2 study initiated in 1Q2019<br>• Simplified regulatory approval pathway via existing nitric oxide NDA<br>• Patent portfolio provides coverage up to 2039 as well as potential for 7-10 years of orphan exclusivity |
| Financial Summary | • IPO on Nasdaq in February 2015<br>• Cash & Equivalents: $20.7M(1), No Debt(1)<br>• Shares Outstanding = 68.9 million(1); Fully Diluted = 110.2 million(1) |

Notes: (1) As of March 31, 2019 per Quarterly Report on Form 10-Q filed May 9, 2019

# INOpulse Delivery System Overview

## Portable Delivery System Allows Chronic iNO Therapy




Nitric Oxide is a well established vasodilator approved for acute treatment of persistent pulmonary hypertension in hospitals

Portable pulsatile iNO delivery system for chronic administration

INOpulse®

Novel drug-device combination therapy with dual mechanisms of action

*Targeted pulmonary vasodilation*

*Ventilation/Perfusion (V/Q) matching*

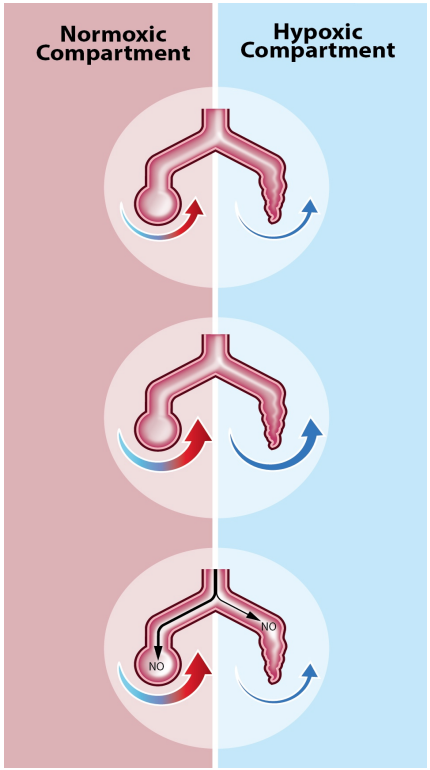
Hospital based continuous flow iNO delivery system for acute administration


INOmax®

Ikaria commercial platform sold to Mallinckrodt for $2.3B

*Approved for use in persistent pulmonary hypertension in neonates*

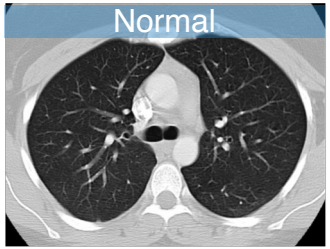
# INOpulse Provides a Unique and Differentiating Mechanism of Action

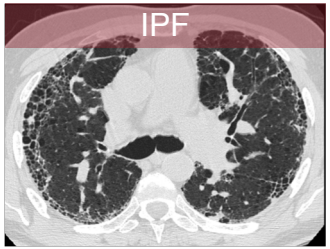



| | |
|---|---|
| **Baseline** | Hypoxic pulmonary vasoconstriction prevents oxygen desaturation |
| **Systemic Vasodilators** | Systemic vasodilators can reverse hypoxic vasoconstriction leading to ventilation/perfusion (V/Q) mismatch and arterial O2 desaturation |
| **INOpulse** | Providing iNO early in the inspiratory phase allows for targeted vasodilation of only the well ventilated alveoli thereby preventing V/Q mismatch and O2 desaturation |

# PH Associated with ILD is Unmet Medical Need with Significantly Reduced Survival

## Interstitial Lung Disease (ILD) is a broad category of diffuse lung diseases characterized by variable amounts of inflammation and fibrosis



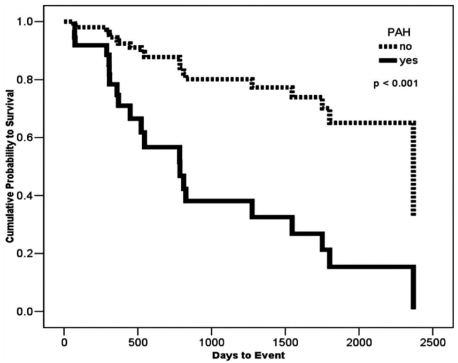




Idiopathic Pulmonary Fibrosis (IPF) is the largest and most serious of the many fibrotic subsets of ILDs

Patients with pulmonary fibrosis have thickening and scarring of the air sacs in the lungs, and often require supplemental oxygen to maintain adequate oxygen saturation

## Prognosis and survival are significantly worse for patients with pulmonary hypertension

**Pulmonary hypertension as predictor of survival in IPF**



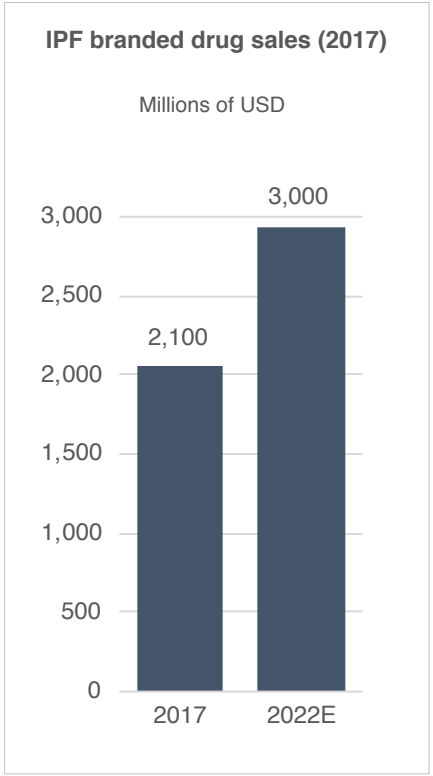

Approximately 40% of IPF patients exhibit symptoms of pulmonary hypertension at rest, including elevated pulmonary pressures

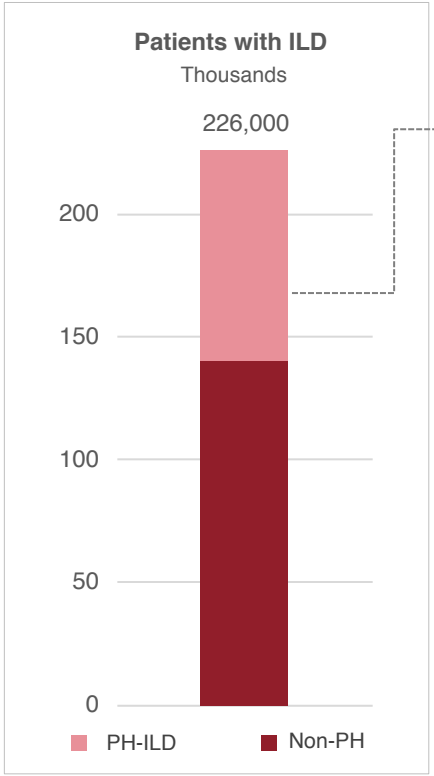
PH-IPF associated with a 3-fold increase in risk of death compared to IPF alone

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

# PH-ILD Market Opportunity in the US




## PH-ILD Patient Population (US)

### ~85,000 PH-ILD in US

- ~40,000 IPF (~40% of total IPF)
- ~45,000 non-IPF (~35% of total non-IPF ILDs)

### Target US penetration ~24,000

- LTOT penetration of 70-75%
- Physician adoption rate of 35-60% for moderate to severe patients.

### $2B+ US Market Opportunity

- KOL feedback supports high unmet medical need in PH-ILD
- Pricing assessment supported by current IPF and PAH therapies priced at $100-200k/year

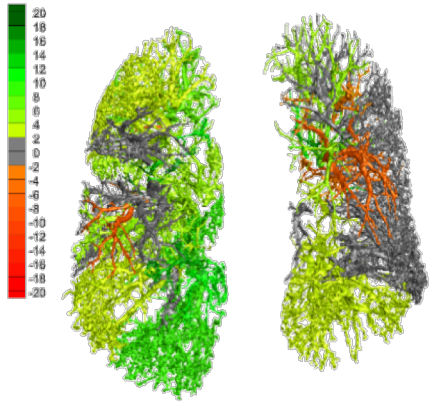
Source: LEK report

# Phase 2a Study PH-IPF

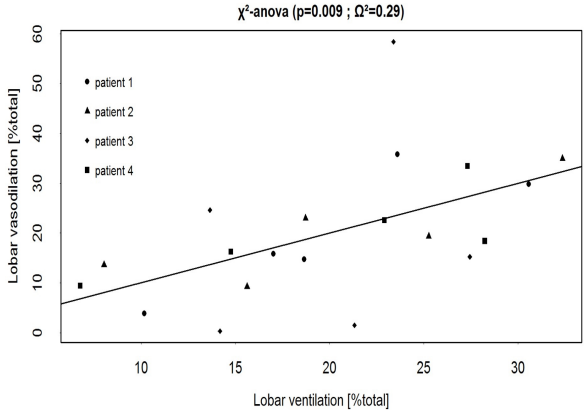
## Acute Phase Data Showed Immediate Benefit of iNO on Vasodilation and Hemodynamics

- 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



# Summary of Key Outputs from iNO-PF Cohort 1 of Phase 2/3 Trial

| | iNO | Placebo | Placebo Corrected Change | |
|---|---|---|---|---|
| MVPA (Moderate to Vigorous Physical Activity; e.g. walking, stairs, yardwork) | +8.1% | -26.1% | +34.2% | • Statistically significant improvement as compared to placebo (p=0.04)<br>• Primary endpoint for pivotal Phase 3 cohort |
| Overall Activity (measured in activity counts) | +0.0% | -11.9% | +11.9% | • Statistically significant improvement in overall activity as compared to placebo (p=0.05) |
| NT-ProBNP (% change) | +15.6% | +42.9% | -27.3% | • Peptide marker indicator of cardiac failure<br>• Larger increase in placebo indicative of disease worsening |
| Oxygen Desaturation | -9.3% | 10.5% | -19.8% | • Lower desaturation for iNO=better saturation |
| SpO2 Nadir | +0.3% | -1.4% | +1.7% | • Higher nadir for iNO=better saturation |

- Results show iNO provides statistically significant improvement in activity as measured by a wearable medical-grade activity monitor (Actigraph GT9X)
- Changes in NT-ProBNP are consistent with activity results, showing greater worsening for placebo subjects
- Unlike other approved PAH systemic vasodilators; INOpulse targeted delivery improves oxygen saturation during exercise

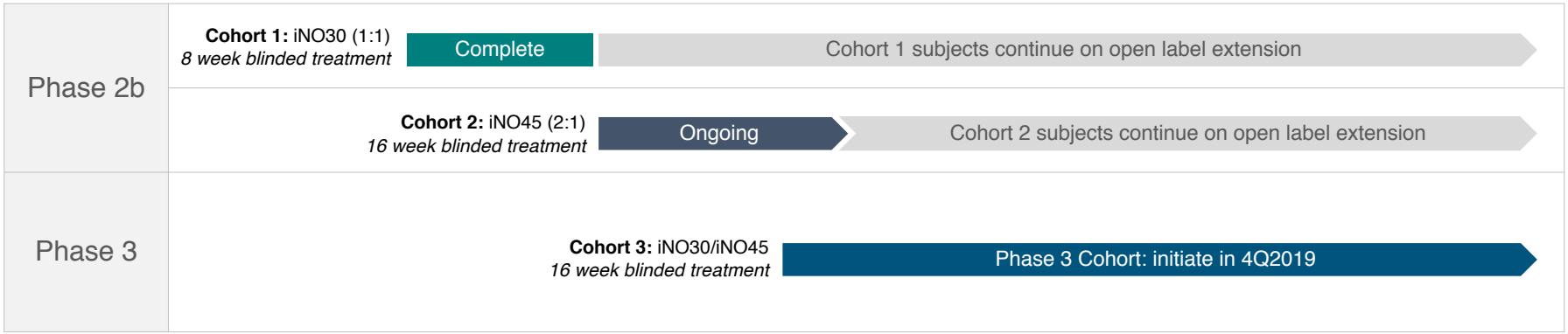
# Phase 2/3 (iNO-PF) Study Allows Seamless Transition into Pivotal Phase 3 Cohort

## FDA agreement on modification of Cohort 3 into pivotal Phase 3 study with MVPA (moderate to vigorous physical activity) as primary endpoint

Double-blind placebo controlled study will assess subjects with pulmonary fibrosis at low or intermediate/high risk of associated pulmonary hypertension

- Cohort 1 results showed statistically significant improvement in MVPA and other activity and cardiopulmonary endpoints
- Cohort 2 is ongoing to assess higher dose (iNO 45) and longer duration of treatment (16 weeks) – readout expected in 2H2019
- Cohort 3 is Phase 3 cohort using MVPA as primary endpoint – to be initiated in 4Q2019

### iNO-PF Phase 2/3 Study Design



# Development Pipeline

| Indication | Market | Development Stage | | |
|---|---|---|---|---|
| | | 2018 | 2019 | 2020 |
| **PH-ILD** (WHO Group 3) | 220,000 with ILD in US<br>35-40% with associated PH<br>Unmet medical need<br>$2B+ potential market | iNO-PF Phase 2b Cohort 1 | iNO-PF Phase 2b Cohort 2 | iNO-PF Phase 3Cohort 3 |
| **PH-COPD** (WHO Group 3) | 12.7 million COPD in US<br>~27% with associate PH<br>Unmet medical need<br>Multi billion dollar potential market | | | PH-COPD Phase 2b |
| **PH-Sarc** (WHO Group 5) | 200,000 with sarcoidosis in US<br>Up to 30% with associated PH<br>Unmet medical need<br>$1B+ potential market | | PH-Sarc Phase 2 | |

## Key Milestones

**Phase 2a Trial completed**
Results presented in May 2017

**Seamless Phase 2/3 iNO-PF Trial**
Positive Cohort 1 results presented in Jan 2019
Cohort 2 ongoing with TLR in 2H2019
Phase 3 Cohort to be initiated in 4Q2019

**Phase 2a Trial completed**
Trial completed in Sept 2017

**Phase 2b Trial: iNO-COPD**
Trial design finalized
Timing TBD

**Phase 2 Trial**
Initiated in 1Q2019

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