Bellerophon Therapeutics

COVID-19 Overview I March 2020

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	• Focused on developing inhaled nitric oxide (iNO) based therapies for outpatient management of chronic cardiopulmonary diseases and COVID-19 • Portable, lightweight delivery system (INOpulse®) allows for chronic home use • Company spun-off from Ikaria
Novel Therapy Addressing Unmet Medical Needs	• Multiple late stage programs in pulmonary hypertension associated with underlying lung disease (WHO Group 3 & WHO Group 5) • Novel targeted vasodilation provides potential for first approved therapy in intended indications • Simplified regulatory approval pathway via existing nitric oxide NDA • Granted emergency expanded access from FDA for the use of INOpulse in COVID-19
Financial Summary	• Cash & Equivalents: $12.9[1,2], No Debt[1] • Shares Outstanding = 4.6 million[1]; Fully Diluted = 7.5 million[1]

Notes: (1) As of September 30, 2019 (2) Does not include $15.3 million in gross proceeds to be received from registered direct offering priced on March 30, 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

PH-PF	PH-COPD / PH-Sarc	COVID-19
Successful Phase 2 studies in PH-IPF	PH-COPD: Successful Phase 2 study completed	First patient dosed via emergency expanded access
Positive results for Phase 2/3 study in Cohorts 1 and 2	PH-COPD: Phase 2b study design finalized in agreement w/ FDA	Expansion to additional sites ongoing
Pivotal Phase 3 cohort to initiate in 2Q2020 with FDA agreement on primary endpoint	PH-Sarc: Phase 2 results expected in 1H2020	Applying for larger IND to allow patients to enroll into randomized study

Proprietary INOpulse Technology

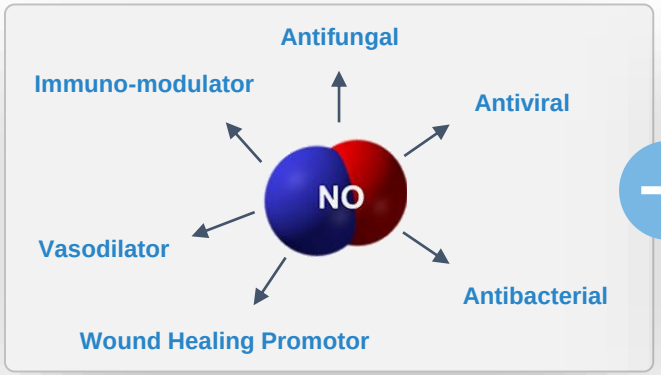
Strong IP protection on core programs through 2033 and ability to extend coverage into 2039

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
Hunter Gillies, M.D. Acting Chief Medical Officer	**20 years** experience in clinical research specializing in cardiometabolic and pulmonary vascular diseases	Pfizer · GILEAD · ACTELION
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	**15 years** of financial experience in medical device and consumer product companies	SYNERON CANDELA · KPMG · Unilever
Parag Shah, PhD VP, Business Operations	**12 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

INOpulse Delivery System Overview

Portable Delivery System Allows Chronic iNO Therapy



INOpulse®

Nitric Oxide

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

Broad spectrum antiviral that plays a key role in suppressing viral replication

Portable pulsatile iNO delivery system

Novel drug-device combination therapy with multiple mechanisms of action

- Targeted pulmonary vasodilation
- Ventilation/Perfusion (V/Q) matching
- Improved oxygen saturation
- Antiviral potential
- Portable delivery system allows out-patient use

INOpulse Delivery System

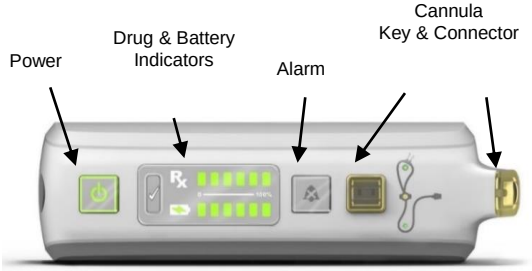
Lightweight, Portable and User Friendly

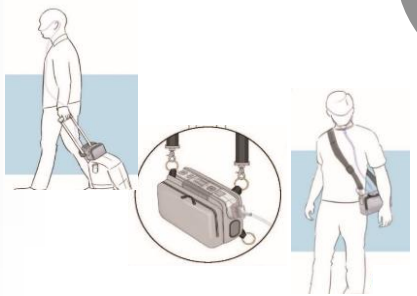
01 Swing engagement with drug cartridge

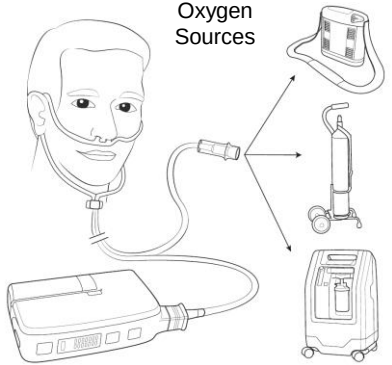
02 Intuitive and simple user interface

03 Tri-lumen cannula allows direct connection with oxygen

04 Lightweight portable design allows ease of transport





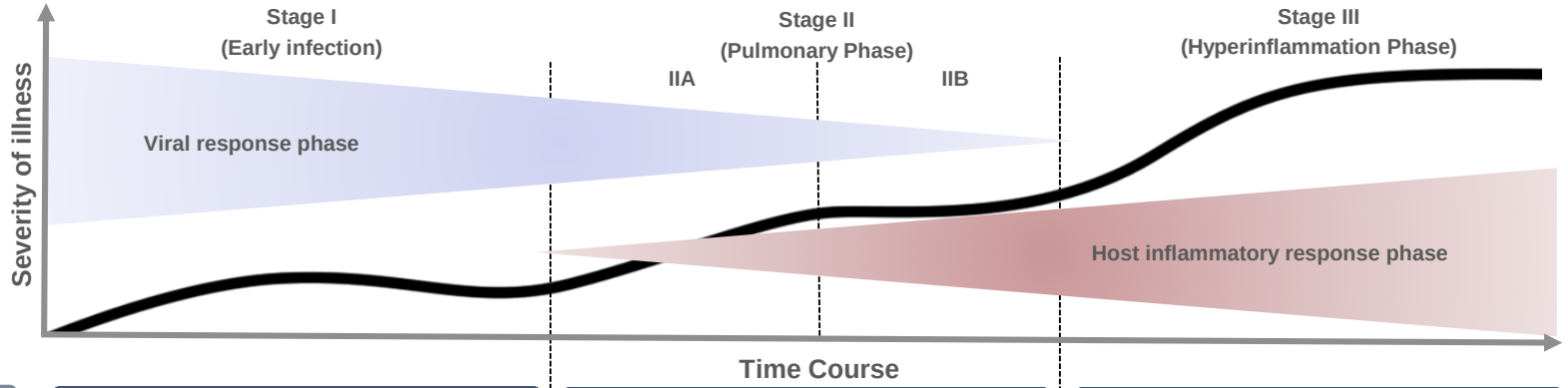


Pulsatile Inhaled Nitric Oxide: Potential Treatment Option for COVID-19

- FDA granted emergency expanded access for pulsatile inhaled nitric oxide for treating Coronavirus (COVID-19); first patient has initiated treatment
    - Also known as compassionate use, administered on a per-patient basis, at times when clinical trials are infeasible and there are no available alternatives
- Inhaled nitric oxide has demonstrated potential benefit for SARS Coronavirus (SARS-CoV) which has genetic similarities to COVID-19
    - NO reduces the viral load and prevents replication of SARS-CoV in vitro
    - iNO improves arterial oxygenation, reduces need for ventilation support, and reduces pneumonia infiltrates in patients with SARS-CoV
- INOpulse delivery system is designed for outpatient use, which may be critical to preventing the further spread and alleviating the mounting impact on hospitals and intensive care units
- Bellerophon has over 200 patient years of data verifying the ability to safely dose pulsatile inhaled nitric oxide needed to provide antimicrobial and antiviral activity

COVID-19 Treatment Paradigm

Inhaled Nitric Oxide: Potential Therapy for Stage II Patients



Clinical Symptoms	Mild constitutional symptoms Fever > 99.6ºF Dry Cough, diarrhea, headache	Shortness of Breath Hypoxia (PaO2/Fi02≤300mmHg)	ARDS SIRS/Shock Cardiac Failure
Clinical Signs	Lymphopenia, increased prothrombin time, increased D-Dimer and LDH (mild)	Abnormal chest imaging Transaminitis Low-normal procalcitonin	Elevated inflammatory markers (CRP, LDH, IL-6, D-dimer, ferritin) Troponin, NT-proBNP elevation
Potential Therapies		INOpulse 	
	Remdesivir, chloroquine, hydroxychloroquine, convalescent plasma transfusions		
	Reduce immunosuppression	Corticosteroids, human immunoglobulin, IL-6 inhibitors, IL-2 inhibitors, JAK inhibitors	

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Image recreated from H. Siddiqi et al., COVID-19 Illness in Native and Immunosuppressed States: A Clinical-Therapeutic Staging Proposal, *J. of Heart and Lung Transplantation*, **2020**, DOI: 10.1016/j.healun.2020.03.012

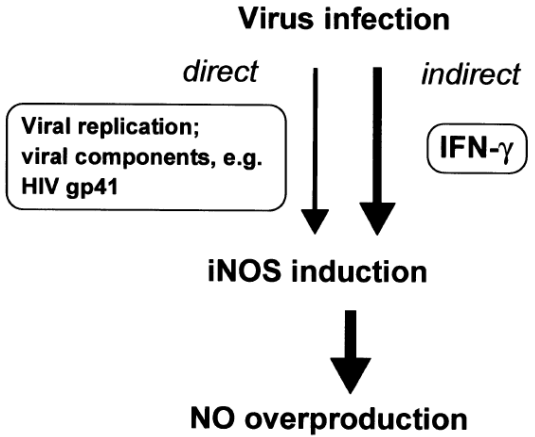
Nitric Oxide Plays a Key Role in Suppressing Viral Replication

Naturally produced immune response to invading pathogens

Endogenous NO production is upregulated by macrophages as a defense mechanism against pathogen infections

Virus replication has been shown to correlate with NO production with inhibition of NO synthesis resulting in increased proliferation

Exogenous NO confers the ability to suppress viral replication supporting the necessity and capability for NO to provide a substantial antiviral effect

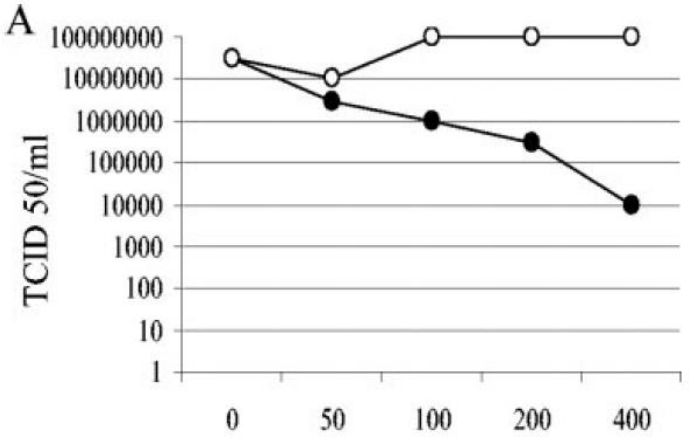


iNOS expression due to viral infection is typically regulated via induction of pro-inflammatory cytokines such as interferon-γ (IFN-γ). In some cases, such as HIV gp41, direct iNOS induction may also occur.

T. Akaike et al., *Immunology,* 101, **2000**, 300-308 M.A. De Groote et al., *Clinical Infectious Disease,* 21, **1995**, S162-S165

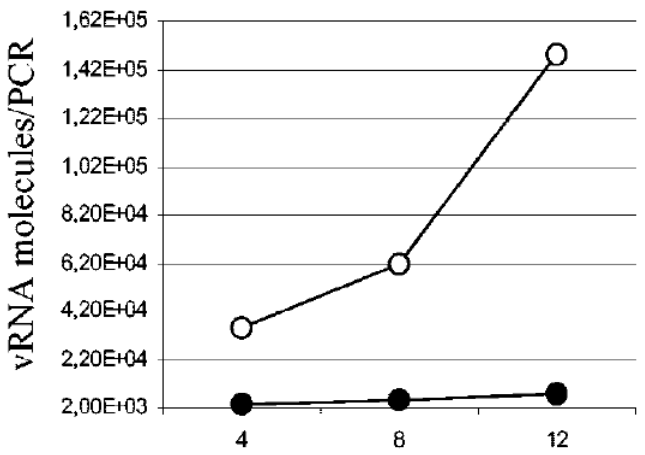
In Vitro Testing Verifies Antiviral Effect of NO on SARS Coronavirus

SNAP (NO donor) reduces viral load and inhibits viral replication of SARS-CoV



SNAP (NO donor) reduces viral load after 24 hours

Cells infected with SARS CoV and treated with different concentrations of NO donor (S-nitroso-N-acetylpenicillamine - SNAP ●) and control (N-acetylpenicillamine - NAP ○)



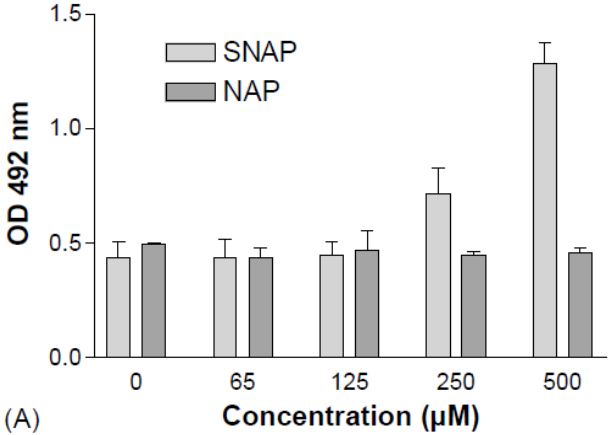
SNAP (NO donor) stops RNA production

Cells infected with SARS-CoV and treated with 400µM NO donor (S-nitroso-N-acetylpenicillamine - SNAP ●) or control (N-acetylpenicillamine - NAP ○); hpi = hour post infection

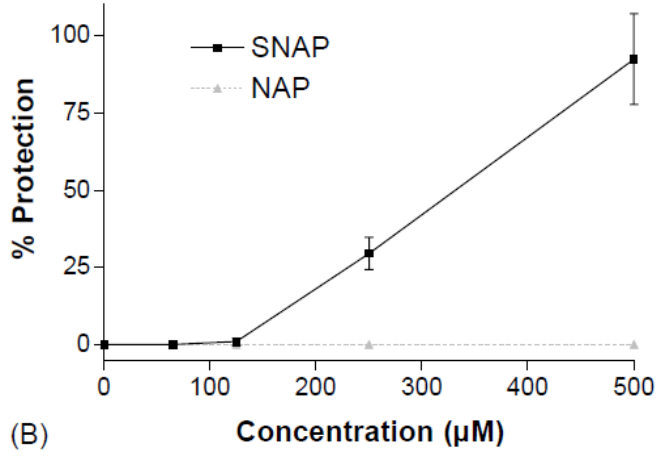
S. Akerstrom et al., *J. of Virology*, 79, **2005**, 1966-1969

NO Improves Survival of SARS Infected Cells

SNAP (NO donor) concentration over 250μM improves cellular survival



Increased survival rate of SARS infected cells by the treatment of SNAP. Optical density (492nm) was measured to determine mitochondrial activity. Data are expressed as means ± S.D.

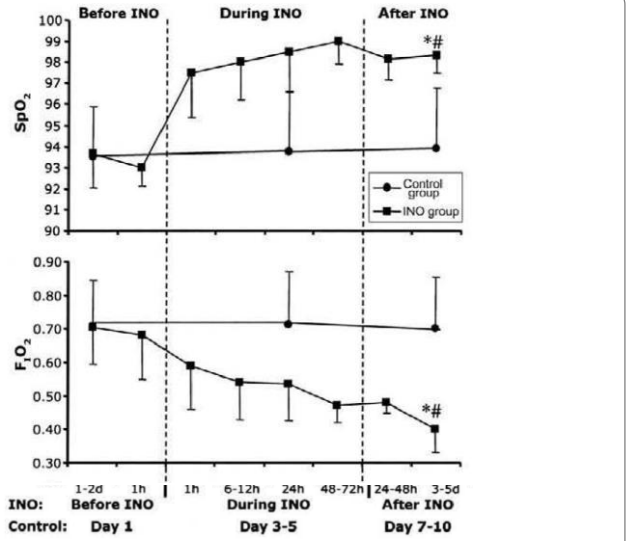


Percent protection achieved in SARS-CoV infected cells. Bars indicate SD.

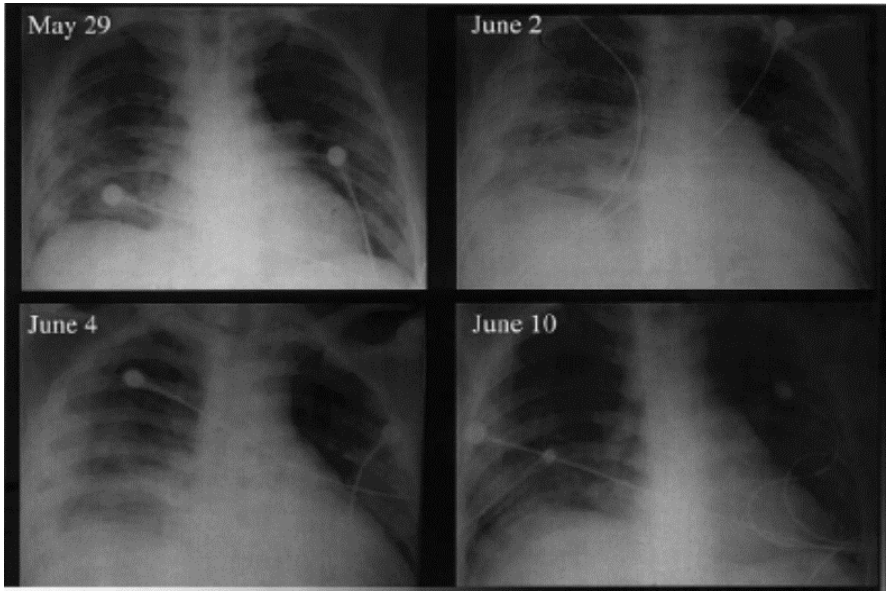
E. Keyaerts et al., *Int. J. of Infectious Disease*, 8, **2004**, 223-226

Inhaled NO Provides Benefit in Patients Infected with SARS-CoV

iNO improves arterial oxygenation and reduces pneumonia infiltrates in SARS patients



Patients demonstrated improved arterial oxygenation and reduced need for ventilation support

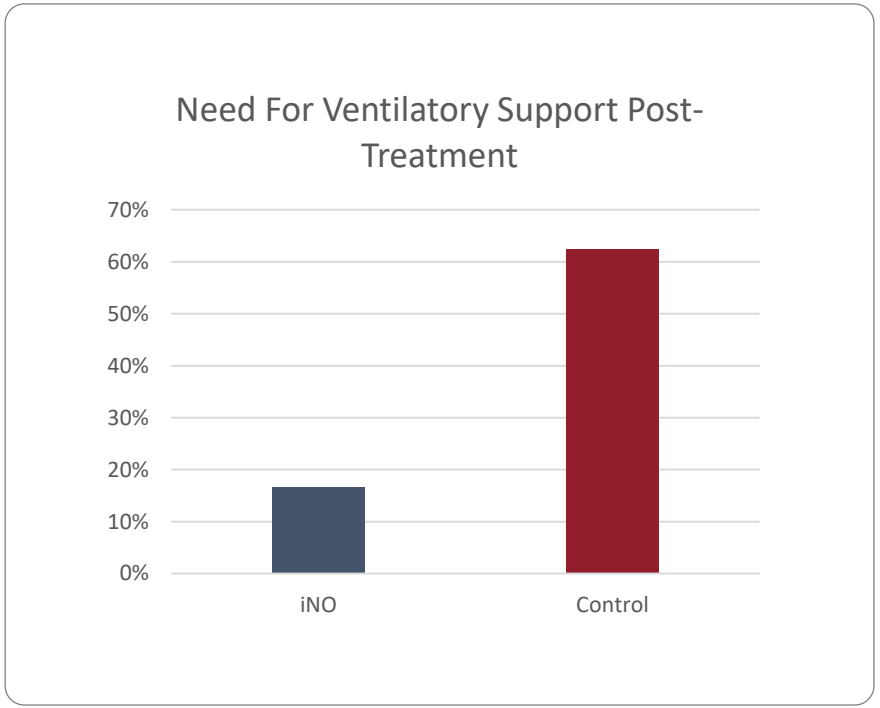


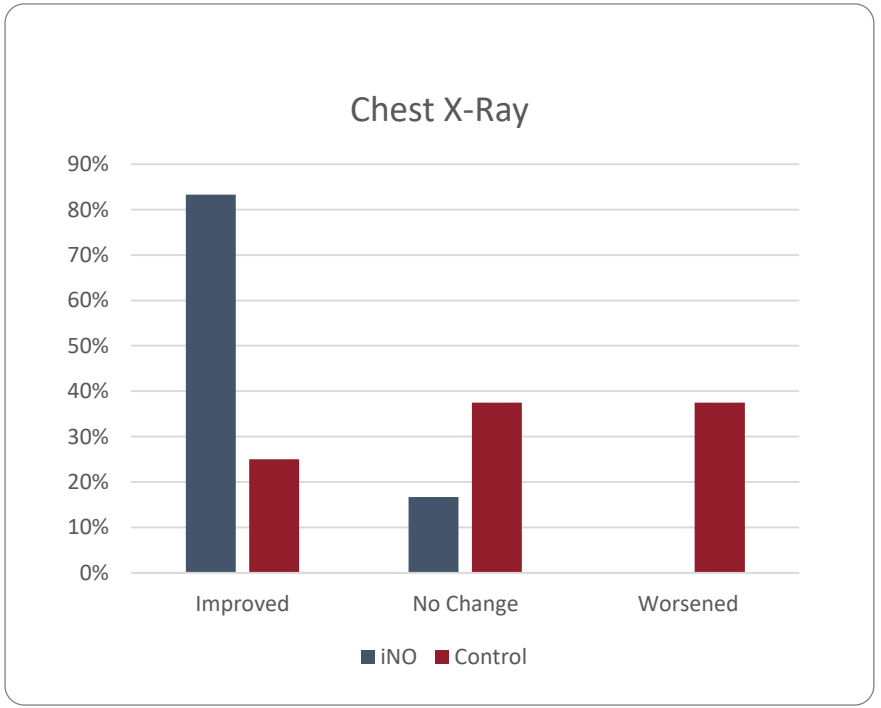
Progression of pneumonia (May 29-June 2); Effect of iNO therapy demonstrating a decrease in the pneumonia infiltrates (June 4 – 10)

L. Chen et al., *Clinical Infectious Disease*, 39, **2004**, 1531-1535

Inhaled NO Provides Benefit in Patients Infected with SARS-CoV

iNO reduces need for mechanical ventilation post-treatment and improves chest x-ray





L. Chen et al., *Clinical Infectious Disease*, 39, **2004**, 1531-1535

Next Steps in COVID-19

FDA has granted emergency expanded access to allow pulsatile inhaled nitric oxide to be used as supportive treatment for COVID-19

Access allows treatment under the care and supervision of a physician on a named patient basis, with first patient dosed in March 2020

Bellerophon is in process of applying for a larger IND to allow patients to be enrolled into randomized study:

Study Population: Patients with suspected or diagnosed COVID-19 who require supplemental oxygen

Study Objective: Verify the safety and efficacy of inhaled nitric oxide in subjects with COVID-19 as determined by:

- Reduction in need for mechanical ventilation, need for intubation, etc.
- Reduction in oxygen requirement or an improvement in oxygen saturation
- Reduction in mortality/morbidity
- Negative conversion of COVID-19 RT-PCR from upper respiratory tract

Study Funding: Engaged in evaluating BARDA and NIH collaborations

Investor Contacts

Fabian Tenenbaum
Chief Executive Officer
BTInvestorRelations@bellerophon.com

Brian Ritchie
LifeSci Advisors
britchie@lifesciadvisors.com
212-915-2578

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