Interim Analysis of INOpulse Pulmonary Arterial Hypertension Long-Term Extension Study (PAH-201)

September, 2015

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.

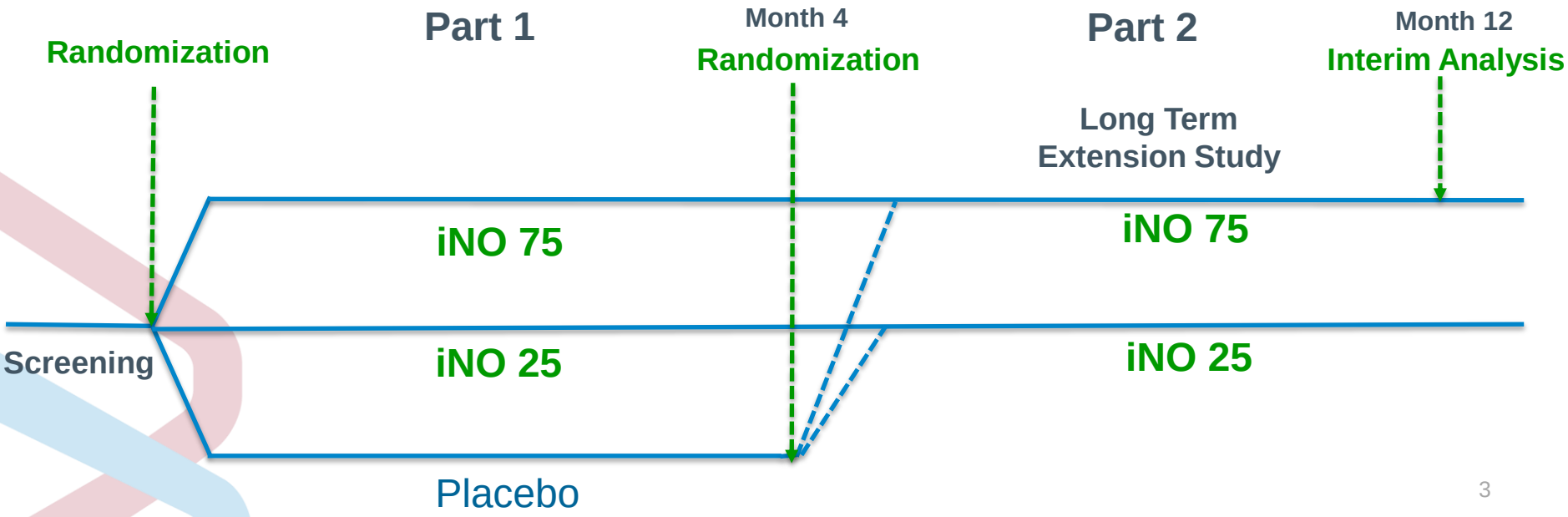
We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking 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.

Part 2 of INOpulse PAH Phase 2 Study

- Following 16 weeks of blinded therapy (Part 1) placebo subjects were randomized to receive either 25 mcg/kg/IBD per hour (iNO 25) or iNO 75; treated patients remained on assigned dose from Part 1
  - 66 patients completed Part 1
  - 65 of 66 entered the Long Term Extension Study (Part 2)

- An Interim Analysis was performed after 12 months from baseline in Part 1
  - 57 subjects with 6MWD data
  - 42 patients with PVR data
  - Data indicates a clinically significant and sustained benefit for patients on iNO 75 when combined with Long Term Oxygen Therapy (LTOT)
  - iNO was generally well tolerated and safety profile is similar to Part 1



Data Collected for Analysis by Group

	6MWD (n)	PVR (n)
iNO 25		
LTOT	16	13
Non-LTOT	10	6
iNO 75		
LTOT	20	14
Non-LTOT	11	9
TOTAL	57	42

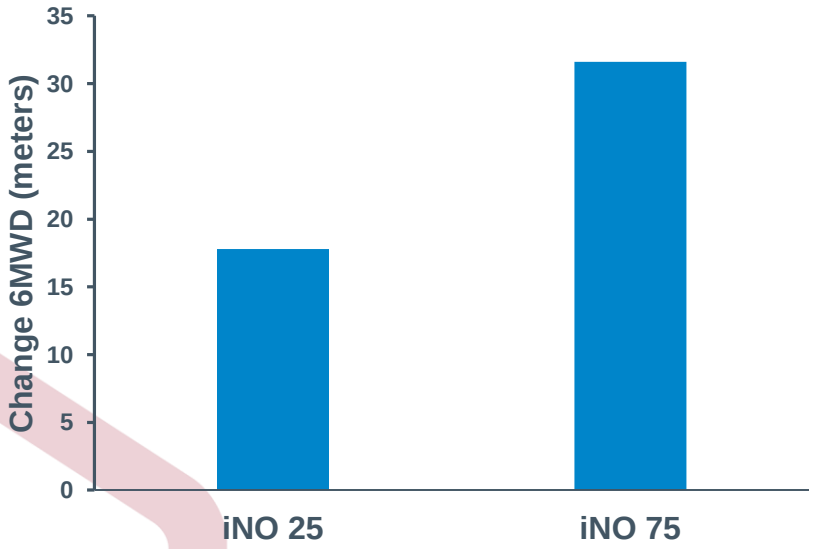
PAH Therapy at Start of Part 2

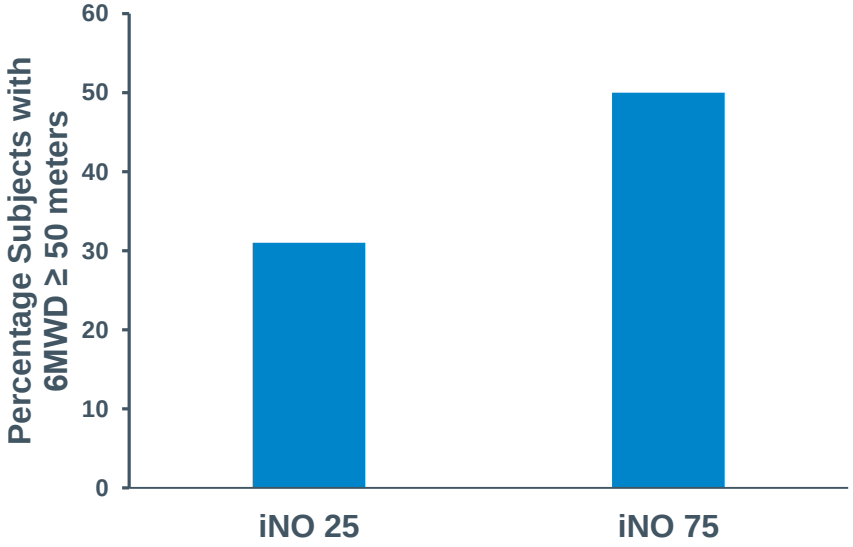
	iNO 25	iNO 75	Total
Monotherapy	9 (28%)	7 (21%)	16 (24%)
Dual Therapy	16 (50%	15 (46%)	31 (48%)
Triple Therapy	7 (22%)	11 (33%)	18 (28%)
IV Prostacyclin	12 (38%)	19 (58%)	31 (48%)

Change in 6MWD with 8 to 12 months of Treatment with iNO 25 and iNO 75 with LTOT

Δ 6MWD (meters)	N	Mean	SE
iNO 25	16	17.8	11.8
iNO 75	20	31.6	13.2

% Δ6MWD ≥ 50 meters	N	%
iNO 25	16	31.3
iNO 75	20	50

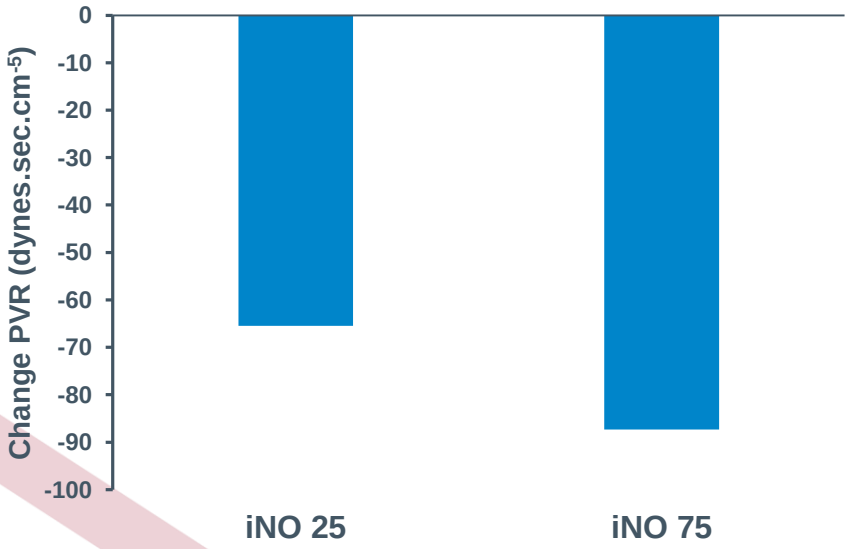


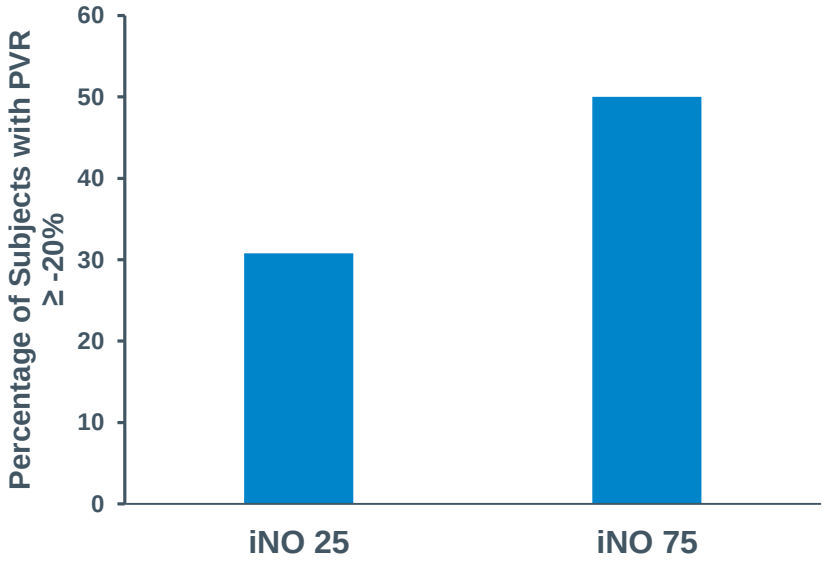


Change in PVR with 8 to 12 months of Treatment with iNO 25 and iNO 75 with LTOT

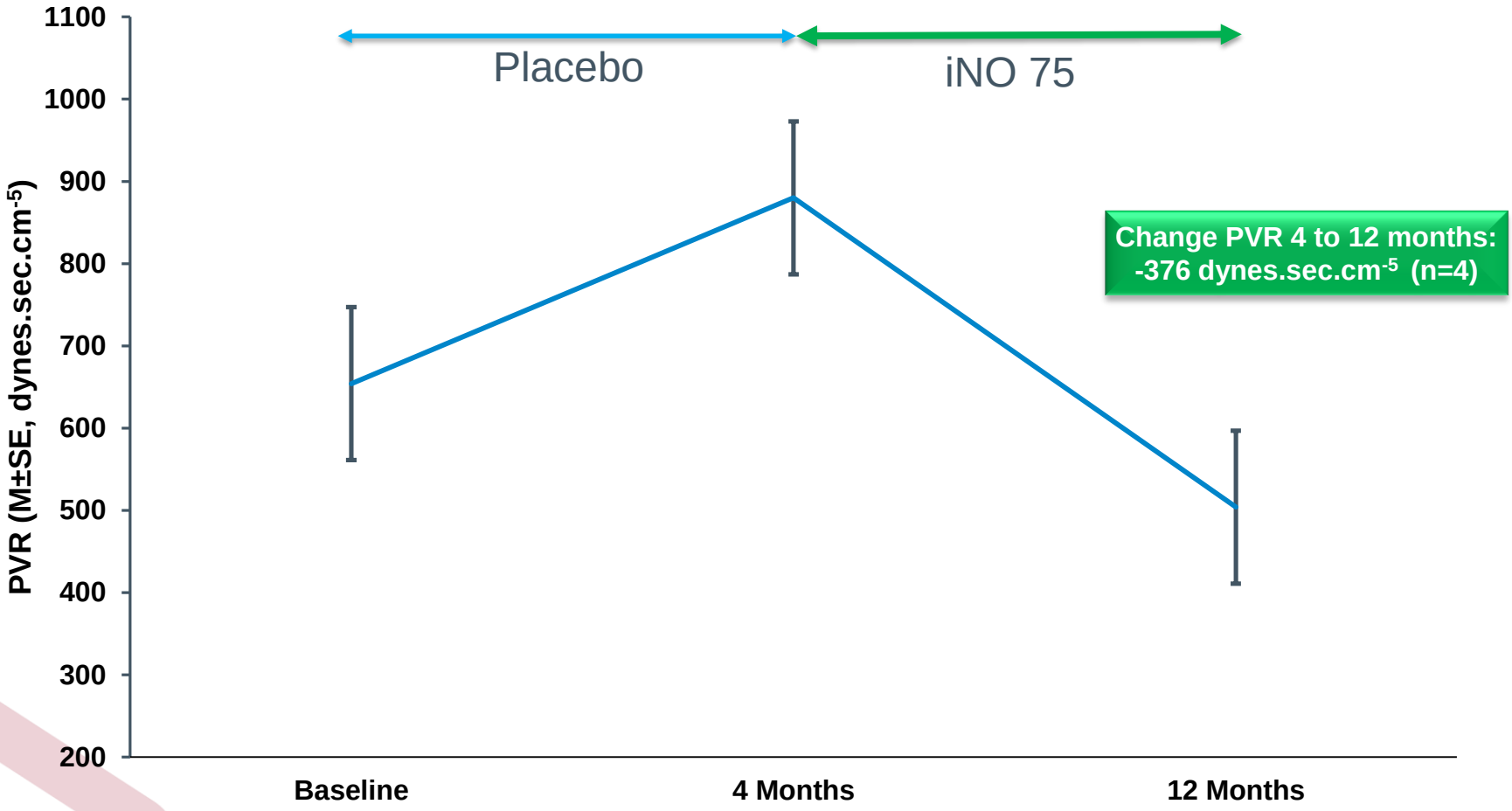
Δ PVR (dynes.sec.cm^{-5})	N	Mean	SE
iNO 25	13	-65.5	48.9
iNO 75	14	-87.3	53.7

Percentage ΔPVR ≥ -20%	N	%
iNO 25	13	30.8
iNO 75	14	50

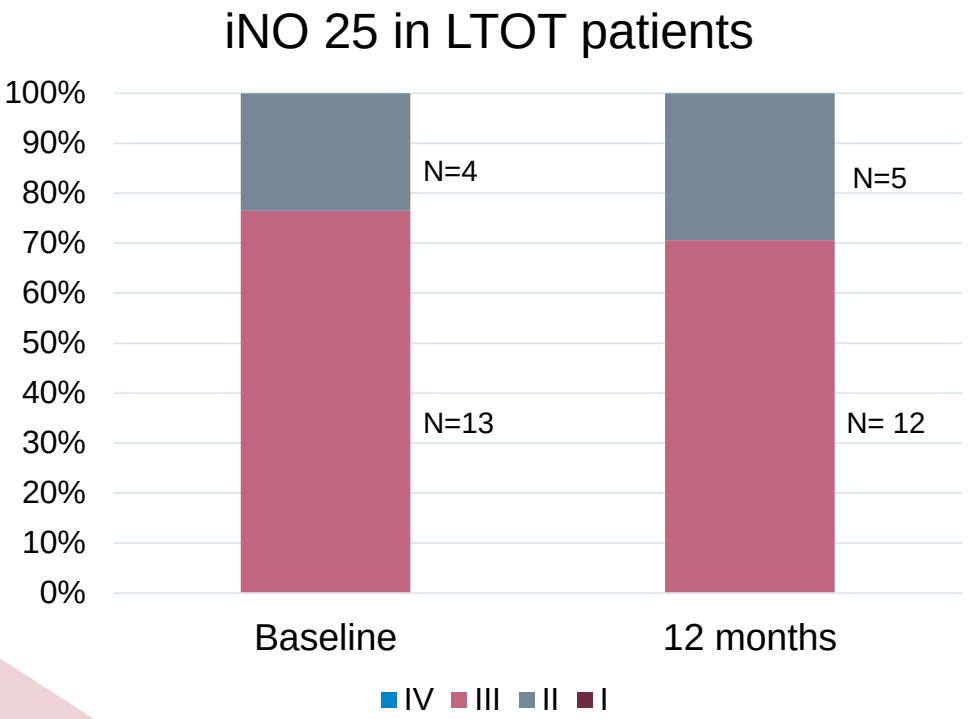


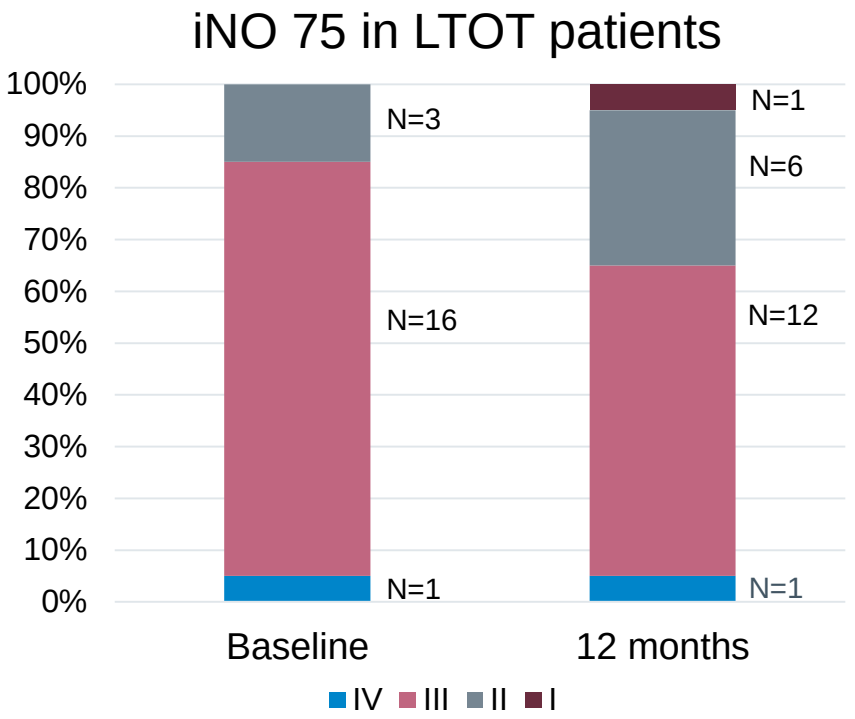


LTOT Patients on Placebo in Part 1 Who Transferred to iNO 75 Did Particularly Well



LTOT Patients on iNO 75 Showed Improvements in WHO Functional Class





LTOT Patients on iNO 75 Who Stayed on Therapy for ≥12 hours a Day Improved Even More

Δ 6MWD (meters)	N	MEAN	SE
iNO 75 < 12 hrs	9	19.6	21.9
iNO 75 ≥ 12 hrs	11	41.4	16.4

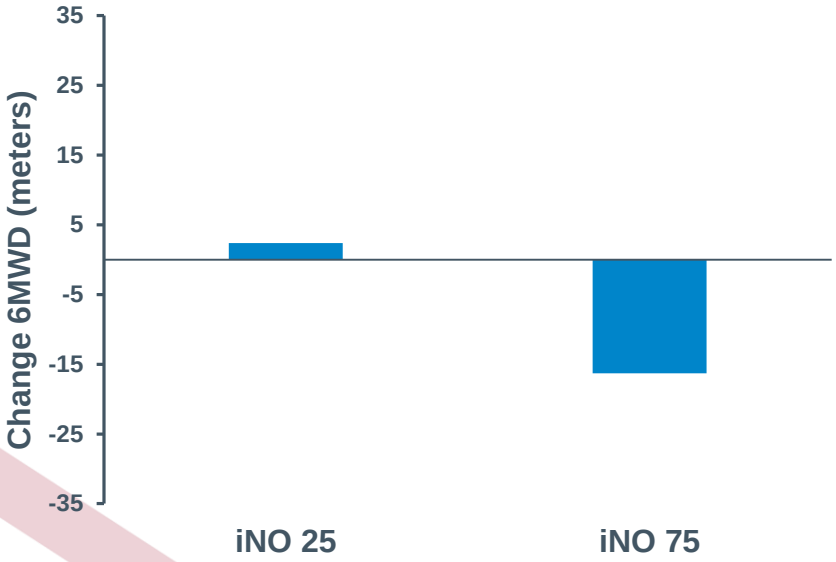
Improvements in 6MWD Were Not Correlated with Changes in PAH Therapies

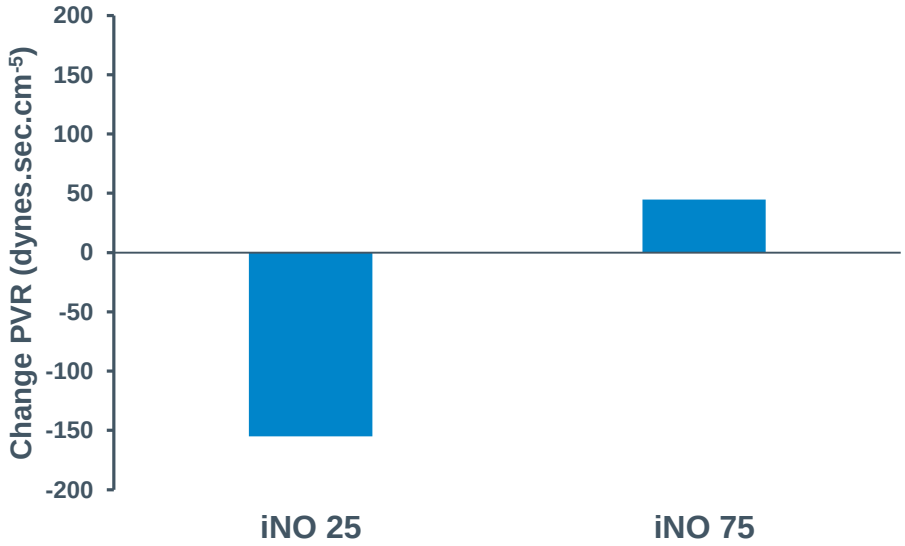
Medications Added in Part 2	iNO 25	iNO 75
Added 1 oral medication	4	0
Added IV prostacyclin	3	0
10% increase in prostacyclin dose	1	0

Inconsistent Results for Patients *Not* on LTOT

Δ 6MWD (meters)	N	Mean	SE
iNO 25	10	2.4	22.7
iNO 75	11	-16.3	18.7

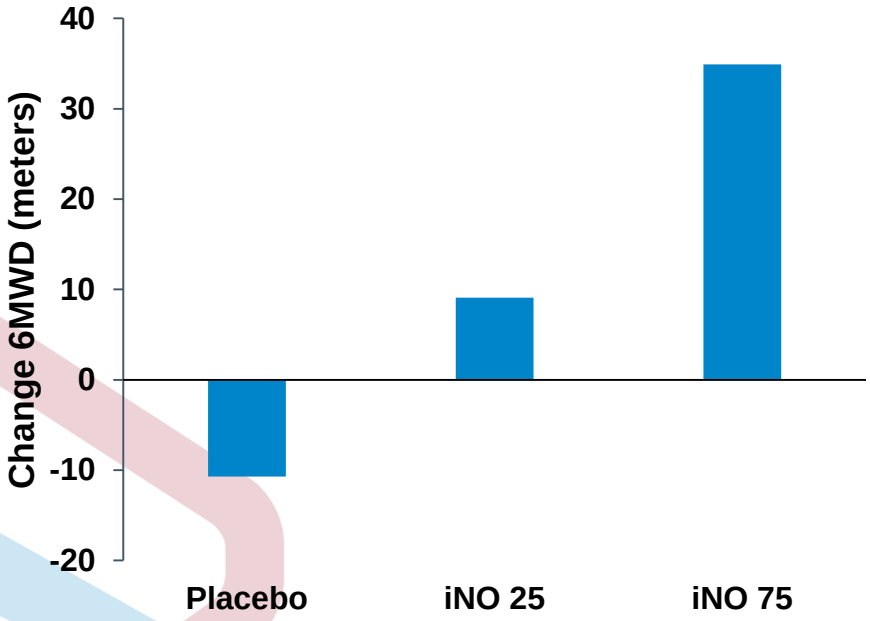
Δ PVR (dynes.sec.cm^{-5})	N	Mean	SE
iNO 25	6	-155	92.5
iNO 75	9	44.8	58.8

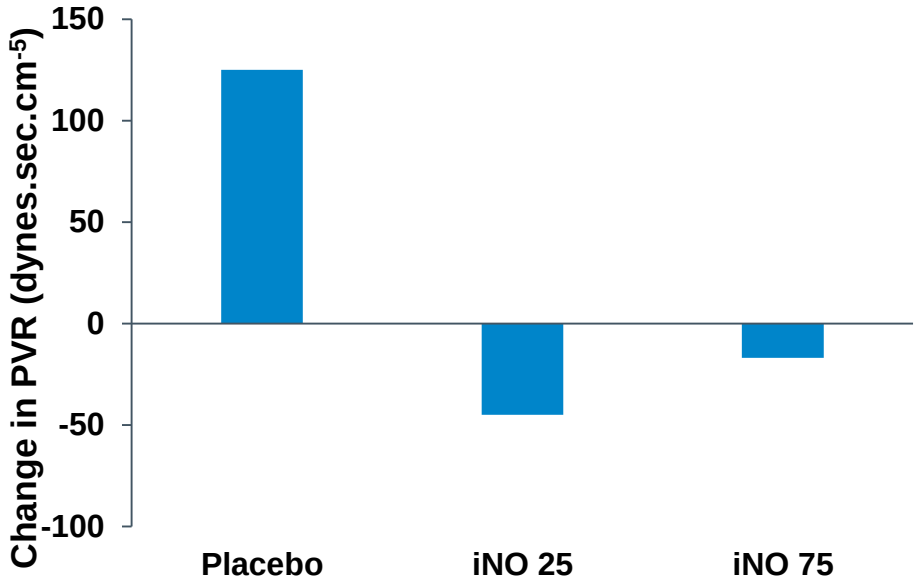




As a Reminder: LTOT Patients on iNO 75 Also Demonstrated Improvement in 6MWD and PVR in Part 1 of the Phase II Study

LTOT Patients	N	6MWD (meters)	PVR (dynes.sec.cm^{-5})
Placebo	10	-10.7	125.5
iNO 25	15	9.1	-47.1
iNO 75	18	34.9	-17.5





* p<0.05 vs. placebo

Hypothesis for Phase III Trial

INOvation
A STUDY OF INHALED NITRIC OXIDE IN PULMONARY ARTERIAL HYPERTENSION

- **The outcome of this interim analysis supports the hypothesis generated in Part 1 of the Phase 2 study**
  - The optimal benefit of iNOpulse is with the iNO 75 dose in patients on LTOT who stay on the therapy for at least 12 hours each day
- **This is the population that will be studied in the Phase III program for which the FDA recently issued a Special Protocol Assessment (SPA)**
  - The European Medicines Agency (EMA) has also agreed to the protocol, through a Scientific Advice Working Party (SAWP)

Phase III Protocol

INOvation
A STUDY OF INHALED NITRIC OXIDE IN PULMONARY ARTERIAL HYPERTENSION

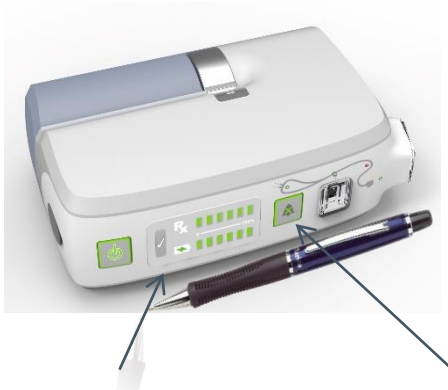
- **Two Trials:**
  - One with 2 arms (iNO 75 and Placebo)
  - One with 3 arms (iNO 75, iNO 50, and Placebo)
  - Each arm will comprise approximately 90 subjects
- **All subjects will be on LTOT**
- **The Primary endpoint is improvement in 6MWD compared to the placebo arm after 16 weeks**
- **The Secondary endpoint is Time to Clinical Worsening (TTCW) with analysis pooled across both trials**
- **Patients will stay on therapy until the last patient last visit**
- **Each trial is 90% powered for a 40 meter improvement in the 6MWD compared to the placebo arm, and for a positive trend on TTCW**
- **Each trial will have a run-in period of 2 weeks to ensure compliance. Subjects who do not stay on the therapy for at least 16 hours a day during this period will be excluded and replaced**

INOpulse Mark 2 is Substantially Lighter and More Intuitive

INOpulse DS

- ~8 lbs. in weight
- LCD display with multiple menus/settings designed for use by RT's in hospital
- Needs a backpack or wheeled bag to carry

INOpulse

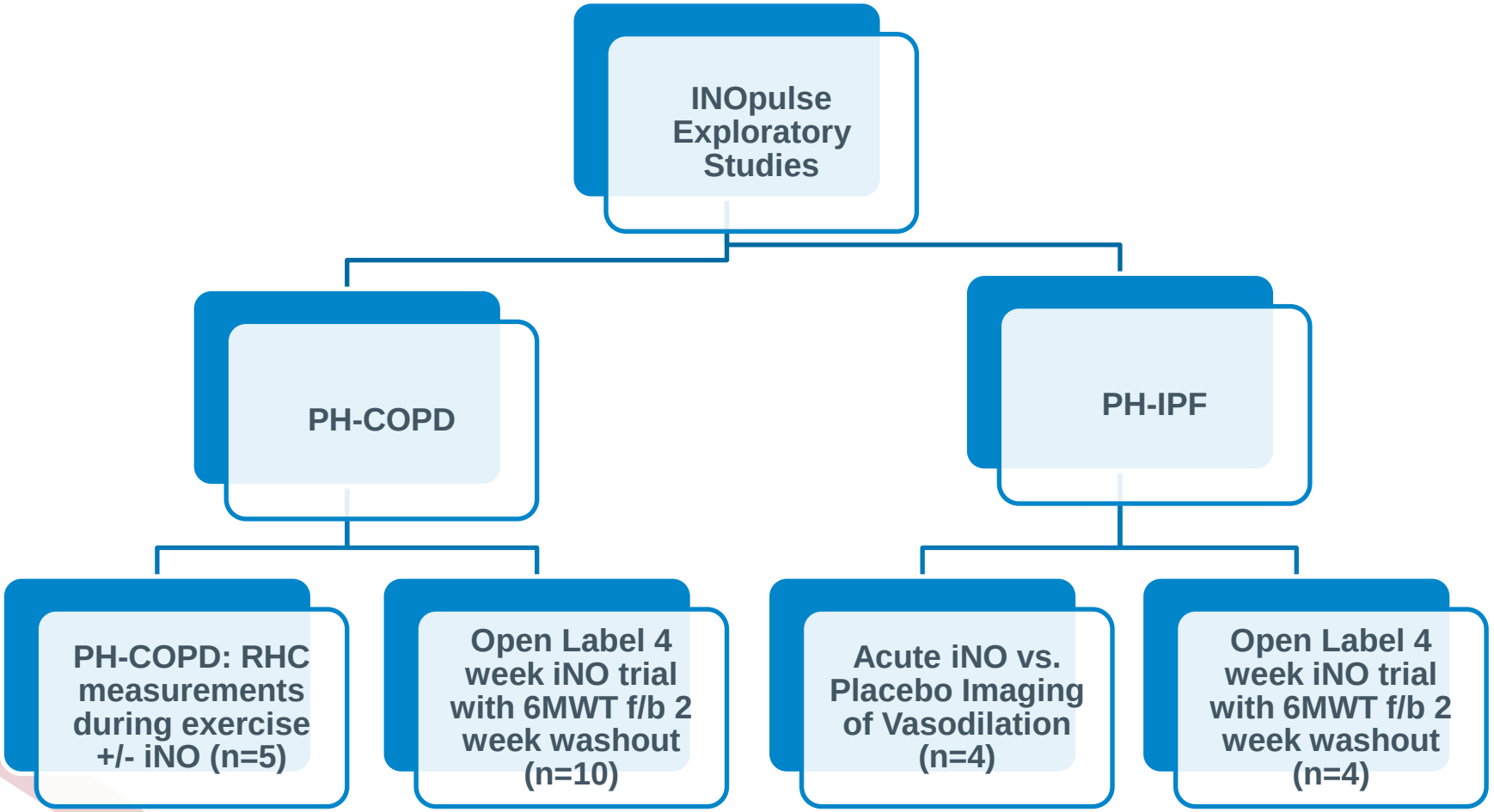


Physicians can set dose and download usage data

- ~2.5 lbs. in weight
- Easy to use user interface
- Fits in small hip/shoulder bag; Per usability testing, patients could carry in purse

Images are not to scale

Additional Work Planned in COPD and IPF in 2015/2016



THANK YOU

Bellerophon™
THERAPEUTICS

Efficacy of Other Approved Drugs for Reference

Ref.	Type of patients	Therapy	Background therapy	Difference from baseline
PAH Specific Background Therapy				
A	NYHA class: III (94%) 12 weeks, n=67	inhaled iloprost	Bosentan	*6MWD* +29* (m)
B	NYHA class: 98% III, 2% IV 12 weeks, n=235	inhaled treprostinil	bosentan or sildenafil	*6MWD* +20 (m) (median)
C	WHO Class: II≈32%, III≈65% 16 weeks, n=341	tadalafil	bosentan (subset)	*6MWD* +19 (m) #
D	WHO Class: II ≈61%, III≈32% 16 weeks, n=587	macitentan	PDE5i or inhaled PGI2	*6MWD* +12.5(m)
E	WHO Class: II=42%, III=53% 12 weeks, n=396	riociguat	ERA or inhaled oral,SC, PGI2	*6MWD* *+29* (m)
No PAH Specific Background Therapy				
F	WHO Class II≈58% III≈41% 12 weeks, n=278	sildenafil (80 mg)	No PAH specific Therapy	*6MWD* +45(m)
G	WHO Class III≈85% IV≈15% *12 weeks, n=32*	bosentan	No PAH specific Therapy	*6MWD* +51(m) (median)
H	WHO Class III≈76% IV≈24% *12 weeks, n= 81*	IV epoprostenol	No PAH specific Therapy	*6MWD* +31(m) (median)
I	WHO Class II≈33% III ≈66 *12 weeks, n=349*	Oral treprostinol	No PAH specific Therapy	*6MWD* +23 (m) (median)

WHO = world health organization, NYHA = New York Heart Association, OL = open label, ERAs = endothelin receptor antagonist, PGI2s = prostacyclin analogues, PDE5Is= phosphodiesterase type 5 inhibitors, ≈ = approximately, * indicates borderline significance (p=0.051), # indicates mean placebo-adjusted response for bosentan subgroup representing add-on treatment

Sources: A = McLaughlin et al. Am J Respir Crit Care Med Vol 174. pp 1257–1263, 2006. B = McLaughlin et al. Journal of the American College of Cardiology Vol. 55, No. 18, 2010. C = Barst et al. J Heart Lung Transplant 2011;30:632–43 D =Pulido et al. N Engl J Med 2013;369:809-18. E =Hossein-Ardeschir Ghofrani, et al. Engl J Med 2013; 369:330-340. F=Galie, et al. N Engl J Med 2005;353:2148-57. G =Channick et al.*Lancet* 2001; 358: 1119–23. H = Barst et al NEJM, 1996;334,296-301 I = Jing, et al.*Circulation*, 2013;127:624-633. J= Data on File