Safety and Tolerability of LIQ861 in Pulmonary Arterial Hypertension (PAH): Results From INSPIRE Study

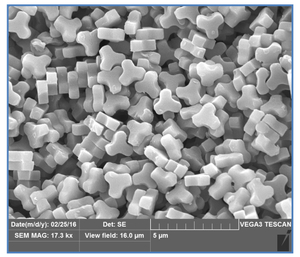
N.S. Hill; J.P. Feldman; S. Sahay; D.J. Levine; S. Patel; A. Galloway; T.M. Bull; on behalf of the INSPIRE study investigators

Research supported by Liquidia Technologies, Inc. Authors' relevant interests: Dr N.S. Hill is a Consultant and Scientific Medical Advisor for Liquidia Technologies and has received grant/research support from Actelion, Bayer, Gilead, Liquidia Technologies, Reata, and United Therapeutics. Dr T.M. Bull is a Consultant and Scientific Medical Advisor for Liquidia Technologies and has received grant/research support from Bayer and Liquidia Technologies.

Introduction[1]

PRINT® Technology results in a uniform size, shape, and chemical composition of dry powder inhalation treprostinil particles.

LIQ861 Dry-Powder Formulation



LIQ861 particles are 1.2 µm in size with trefoil shape

RS00 Model 8 Dry-Powder Inhaler

Compact, disposable inhaler previously approved by FDA and EMEA

Phase 1 PK trial demonstrated that 79.5 mcg of LIQ861 provides comparable systemic exposure to 9 breaths of Tyvaso®.

INSPIRE Study Design[1,2]

Treatment Phase for Primary Endpoint Was Followed by Evaluation for Safety and Tolerability

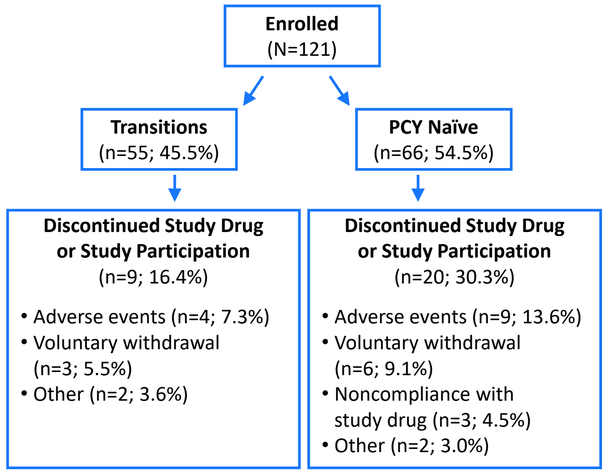
Subjects Overview	• WHO Group I (PAH) NYHA Class II, III, and IV; N≥100 • Divided into 2 groups
Prostanoid-Naïve (PCY Naïve) ≤2 non-PCY oral PAH Rx	• Initiate LIQ861 26.5 mcg capsule strength dose • Increase in 26.5 mcg increments weekly to tolerance and symptom relief
Transitions From Tyvaso® Stable doses ≥3 mo.	• Initiate with comparable dose of LIQ861 • Titrate in 26.5 mcg incremental doses to tolerance and symptom relief
Primary Objective	• Incidence of AEs and SAEs

INSPIRE Study Design (cont'd)[1,2]

Demographics and Baseline Characteristics

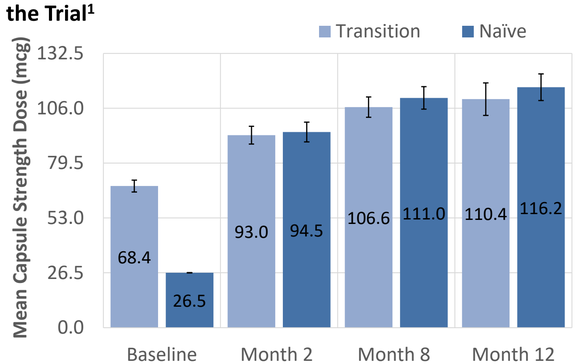
		Transitions (n=55)	PCY Naïve (n=66)	Overall (n=121)
Sex	Female	47 (85.5%)	52 (78.8%)	99 (81.8%)
Age (years)	Mean ± SD	53 ± 14.1	55 ± 14.6	54 ± 14.3
BMI (kg/m²)	Mean ± SD	30.07 ± 7.9	29.31 ± 7.8	29.66 ± 7.8
NYHA Functional Class at Screening	Class II	43 (78.2%)	37 (56.1%)	80 (66.1%)
	Class III	12 (21.8%)	29 (43.9%)	41 (33.9%)
PAH Duration (years)	Mean ± SD	7.25 ± 5.1	4.71 ± 5.1	5.87 ± 5.2
PAH Therapy at Screening	PDE5i alone	8 (14.5%)	12 (18.2%)	20 (16.5%)
	PGI2 alone	6 (10.9%)	-	6 (10.9%)
	ERA alone	5 (9.1%)	3 (4.5%)	8 (6.6%)
	sGC alone	-	2 (3%)	2 (3%)
	ERA + PDE5i	35 (63.6%)	46 (69.7%)	81 (66.9%)
	ERA + sGC	1 (1.8%)	3 (4.5%)	4 (3.3%)

Disposition of Patients



Safety Results[1]

Patients Were Able to Increase the LIQ861 Dose During the Trial[1]



- The median dose of LIQ861 at the end of the study was 106 mcg of treprostinil QID
- At end of the study, one patient achieved a dose of 212 mcg QID (equivalent to approximately 24 breaths of Tyvaso® QID)

AEs Related to Treatment Comprise the Majority of AEs and Are Commonly Seen with Inhaled Prostacyclin Therapy

Most Common AEs (≥4%) Related to LIQ861 Treatment	Overall N=121			
	No. (%) Subjects	No. of Events		
		Mld	Mod	Sev
Cough	58 (48%)	46	12	0
Headache	35 (29%)	25	9	1
Throat Irritation	19 (16%)	18	1	0
Dizziness	14 (12%)	13	1	0
Chest Discomfort	13 (11%)	10	3	0
Diarrhea	12 (10%)	7	5	0
Nausea	9 (7%)	6	2	0
Flushing	9 (7%)	9	0	0
Dyspnea	7 (6%)	4	3	0
Oropharyngeal Pain	6 (5%)	5	0	1

As expected, PCY Naïve patients had a higher rate of AEs related to treatment than Transition patients (85% vs 73%).

Safety Results (cont'd)[1]

Most Common AEs (≥4%) Related to LIQ861 Treatment	Transitions n=55				PCY Naïve n=66			
	No. (%) Subjects	No. of Events			No. (%) Subjects	No. of Events		
		Mld	Mod	Sev		Mld	Mod	Sev
Cough	19 (35%)	17	2	0	39 (59%)	29	10	0
Headache	16 (29%)	12	4	0	19 (29%)	13	5	1
Throat Irritation	5 (9%)	5	0	0	14 (21%)	13	1	0
Dizziness	6 (11%)	5	1	0	8 (12%)	8	0	0
Chest Discomfort	8 (15%)	6	2	0	5 (7%)	4	1	0
Diarrhea	4 (7%)	2	2	0	8 (12%)	5	3	0
Nausea	4 (7%)	3	1	0	5 (7%)	3	1	1
Flushing	3 (6%)	3	0	0	6 (9%)	6	0	0
Dyspnea	4 (7%)	2	2	0	3 (5%)	2	1	0
Oropharyngeal Pain	-	-	-	-	5 (8%)	4	0	1
Vomiting	-	-	-	-	3 (4%)	0	2	1
Fatigue	-	-	-	-	3 (4%)	2	1	0
Pain in Jaw	-	-	-	-	3 (4%)	3	0	0
Lung Disorder	-	-	-	-	3 (4%)	2	1	0

- Twenty-one (17%) patients experienced SAEs
  - No SAEs were deemed as treatment-related by the Medical Monitor
- No clinically relevant findings were observed for:
  - Clinical labs
  - Physical exams
  - Vital signs

Conclusions[1]

LIQ861 in Pivotal Phase 3 INSPIRE Study: Safety and Tolerability at 1 Year

- Other than expected prostanoid-related adverse events, inhaled administration of LIQ861 had no important adverse safety outcome during the INSPIRE trial

Clinical Implication

LIQ861 dry powder formulation of treprostinil provides a safe and tolerable treatment for patients with PAH.

References: 1. Liquidia Technologies data on file. **2.** Investigation of the Safety and Pharmacology of Dry Powder Inhalation of Treprostinil (INSPIRE). ClinicalTrials.gov. January 16, 2018. Updated November 6, 2020. Accessed April 26, 2022. https://clinicaltrials.gov/ct2/show/NCT03399604.

Abbreviations: AE, adverse event; BMI, body mass index; ERA, endothelin-1 receptor antagonist; Mld, mild; Mod, moderate; Sev, severe; Naïve, PCY Naïve; NC, no change; PCY, prostacyclin; PK, pharmacokinetic; QID, 4 times daily; Rx, prescription; SAE, serious adverse advent; SD, standard deviation.

© 2022 Liquidia Technologies, Inc. Tyvaso® is a registered trademark of United Therapeutics Corp.