A Phase 3, Open-Label, Multicenter Study to Evaluate the Long-Term Safety and Tolerability of Inhaled LIQ861 (Treprostinil) in Pulmonary Arterial Hypertension (WHO Group 1) Patients – Month 2 Outcomes. INSPIRE: Investigation of the Safety and Pharmacology of Dry Powder Inhalation of Treprostinil

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Presenter: N.S. Hill

Tufts Medical Center

LIQUIDIA TECHNOLOGIES

Relevant Financial Relationship Disclosure Statement

- **INSPIRE: A Phase 3, Open-Label, Multicenter Study to Evaluate the Safety and Tolerability of LIQ861 in Pulmonary Arterial Hypertension (PAH)**
  - Presenter: N.S. Hill, MD
  - I will discuss investigational use of the following drugs/devices: LIQ861 Dry Powder Inhalation of Treprostinil
- **The following relevant financial relationships exist related to this presentation:**
  - N.S. Hill:
    - Consultant - Liquidia Technologies
    - Grant/Research Support Institution - Actelion, Bayer, Gilead, Liquidia Technologies, Reata, United Therapeutics
    - Scientific Medical Advisor - Liquidia Technologies

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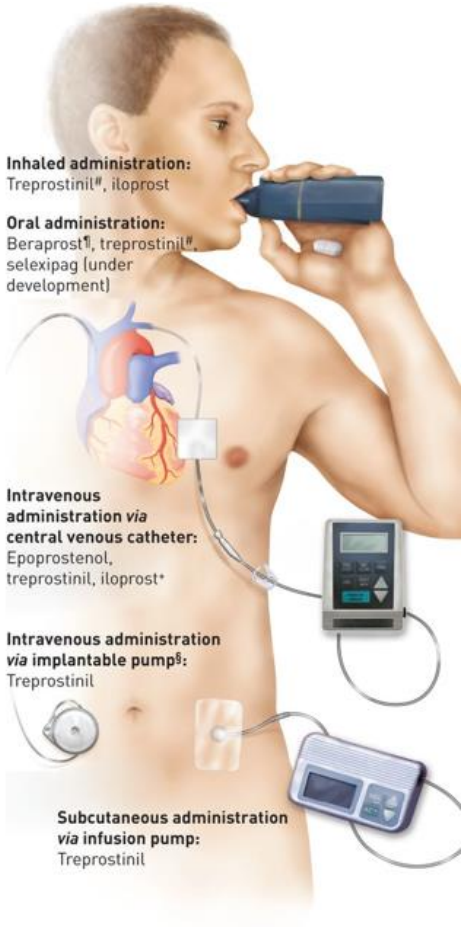
In PAH, Prostacyclin Therapy (PGI2) Improves Symptoms and Limitations by Replacing Deficient Prostacyclin at the Highest Tolerable Level of Drug

Current prostacyclin-based products have clear tradeoffs



Infusion (Continuous IV or SubQ) = Effective, but… systemic toxicities, cumbersome, limitations on lifestyle

- IV poses risk of line sepsis, SubQ limited by site pain

Oral = Convenient, but… toxicities and limited symptom relief

- Increased GI side effects
- Uptitration can be challenging given side effects

Inhaled = Local delivery, but… provides limited dose range

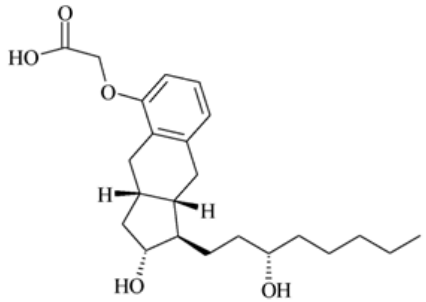
- Due to throat, airway irritation, cough
- Inconvenient; requires assembly, cleaning, and time to administer

Source: Decision Resources, Pulmonary Hypertension Disease Landscape & Forecast, November 2018; Recent advances in targeting the prostacyclin pathway in pulmonary arterial hypertension, November 2015.

Novel PRINT® Technology Results in a Uniform Size, Shape, and Chemical Composition of Treprostinil Particles

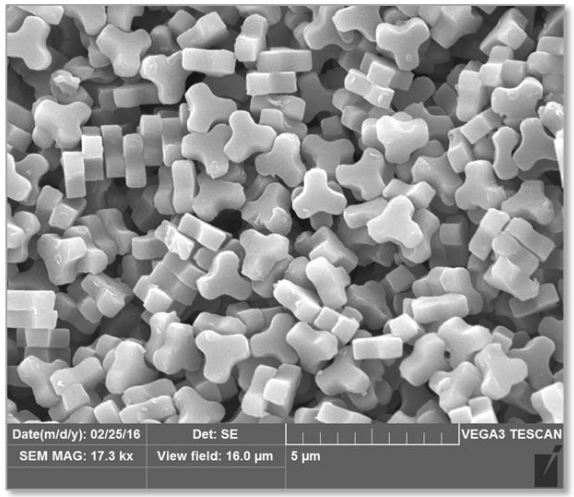
Each identical particle is within the respirable range (<5.0 microns)

Treprostinil



Treprostinil
(prostacyclin analog)

LIQ861 Dry-Powder Formulation



LIQ861 particles are between 1-2 µm wide with trefoil shape

RS00 Model 8 Dry-Powder Inhaler

Compact, disposable inhaler previously approved by FDA and EMEA

Source: Data on file.

INSPIRE Study Design

	Day 0	Week 2	Month 1	Month 2
WHO Group I (PAH) **NYHA Class II, III, and IV** N≥100	**Treatment Phase for Primary Endpoint**			
Add-Ons Prostanoid-Naïve ≤2 non-PGI 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 Endpoint	• **Incidence of TEAEs and SAEs at 2 months**			
Exploratory Endpoints	• Sustained use after transition (Tyvaso® transitions) • 6-minute walk distance • NT-proBNP • NYHA functional class • Quality of life questionnaire/patient satisfaction with LIQ861 • Risk assessment			

PGI = prostacyclin; SAE = serious adverse event; TEAE = treatment-emergent adverse event.
Source: https://clinicaltrials.gov/ct2/show/NCT03399604. Tyvaso® is a registered trademark of United Therapeutics Corp.

Demographics and Baseline Characteristics

		Transitions (n=55)	Add-Ons (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 PGI2 alone ERA alone sGC alone	8 (14.5%) 6 (10.9%) 5 (9.1%) -	12 (18.2%) - 3 (4.5%) 2 (3%)	
	ERA + PDE5i ERA + sGC	35 (63.6%) 1 (1.8%)	46 (69.7%) 3 (4.5%)	

Source: data on file

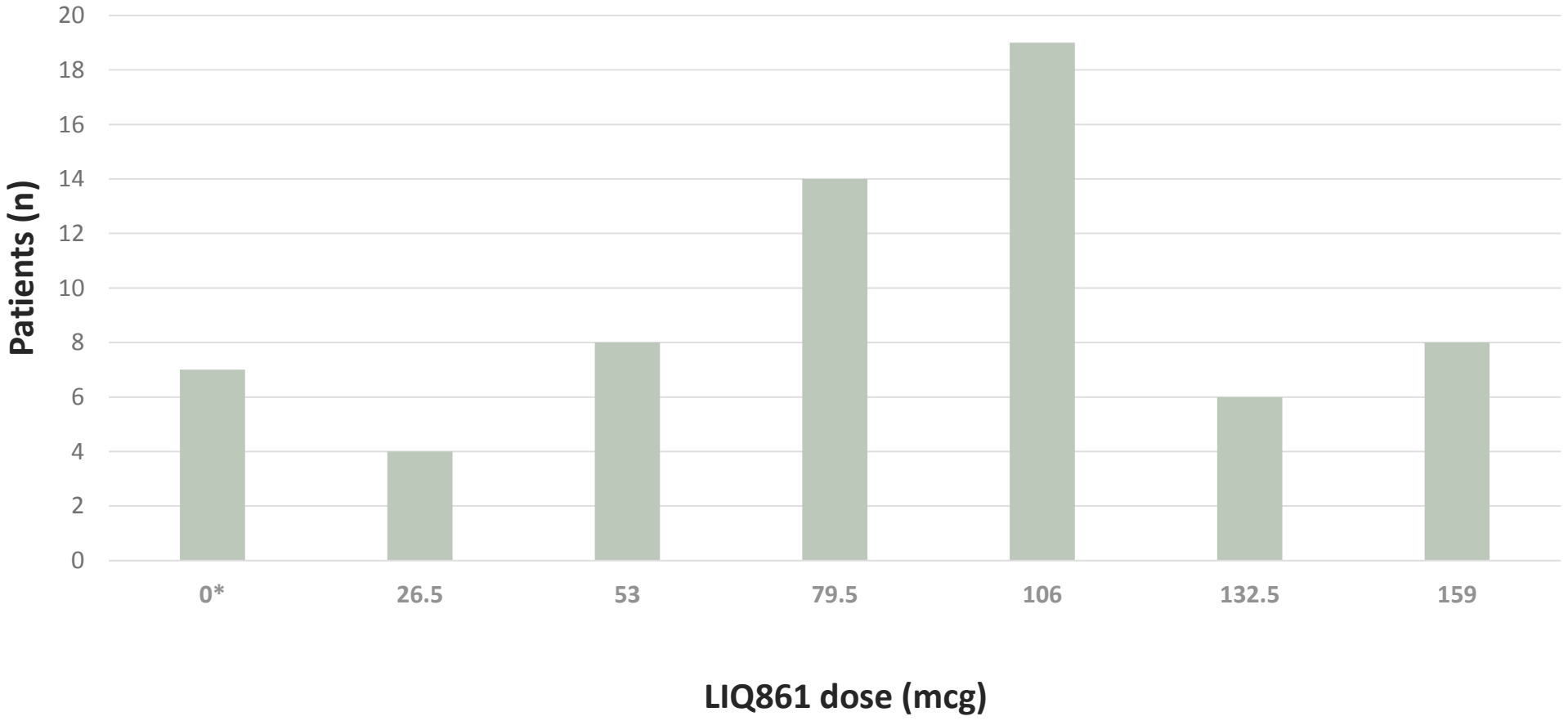
Most Patients Remained on LIQ861 Through 2 Months of Treatment

Sustained Therapy at 2 Months			
	Transitions	Add-Ons	Overall
Total Patients Enrolled	55	66	121
Discontinued ≤2 Months*	5	6	11
Sustained at 2 Months	53	60	113
% Patients Sustained at 2 Months	96.4%	90.9%	93.4%

*Patients discontinued at or prior to Month 2 due to adverse events, patient choice, investigator decision, lost to follow up.
Source: data on file.

LIQ861 Dose at Month 2 in Add-On Population (n=66)

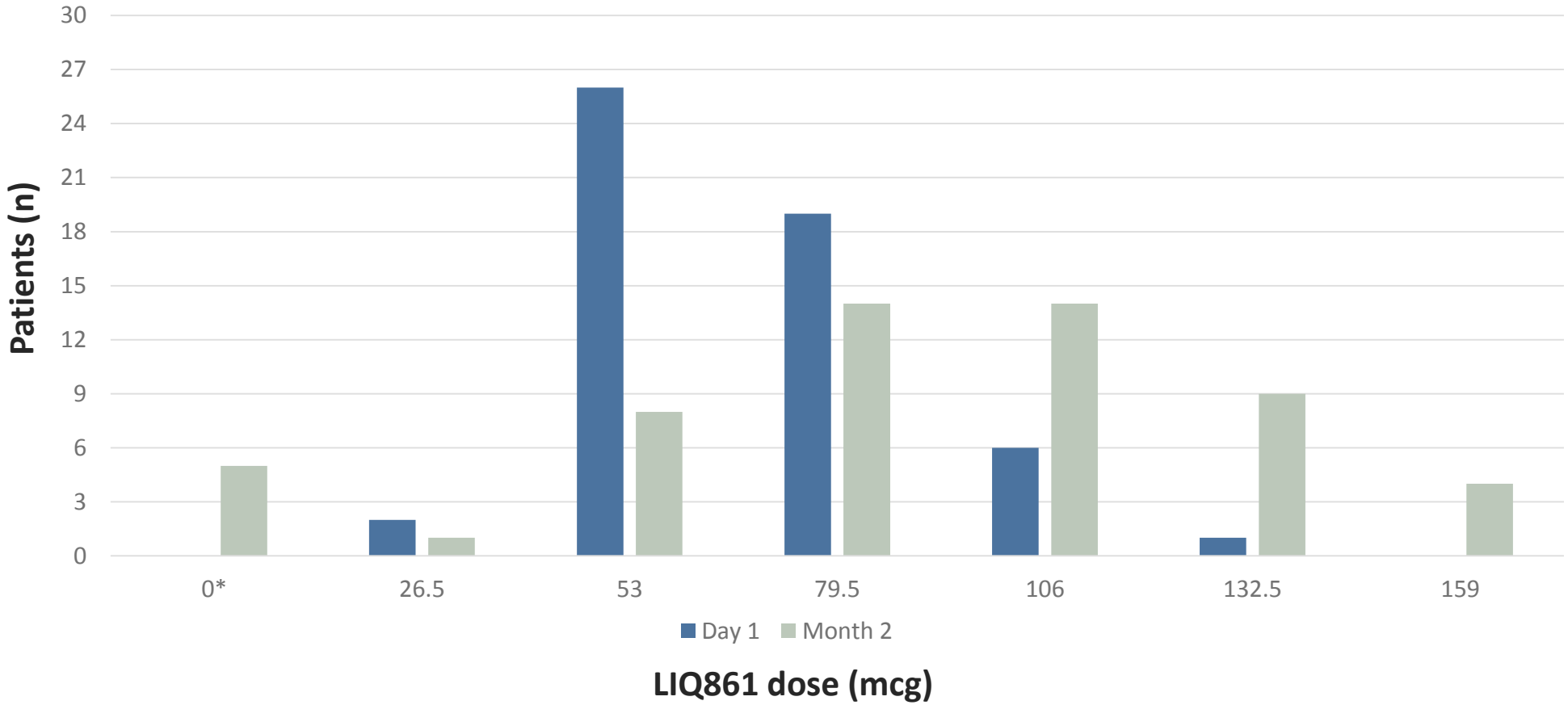
- LIQ861 initial dose: 26.5 mcg
- LIQ861 dose at Month 2: 71% patients titrated to ≥79.5 mcg



*Dose was summarized as 0 mcg if patients had discontinued or if dosing had been temporarily interrupted at the visit
Source: data on file.

LIQ861 Dose at Month 2 in Transition Population (n=55)

- LIQ861 initial dose: 94% patients transitioned to ≥53 mcg
- LIQ861 dose at Month 2: 74% patients titrated to dose ≥79.5 mcg



*Dose was summarized as 0 mcg if patients had discontinued or if dosing had been temporarily interrupted at the visit
Source: data on file.

Serious Adverse Events (SAEs) Unrelated to LIQ861

Respiratory, Thoracic, and Mediastinal disorders

- Acute pulmonary embolism*
- Shortness of breath

Injury, Poisoning and Procedural complications

- Fractured lower leg

Nervous System disorders

- Possible seizure
- Syncope

Gastrointestinal disorders

- Gastrointestinal bleed

*One patient experienced 2 SAEs.
Source: data on file.

Treatment-Emergent Adverse Events (TEAEs) Observed Were Consistent With Inhaled Prostacyclins and Were Generally Mild to Moderate in Severity

Primary Endpoint

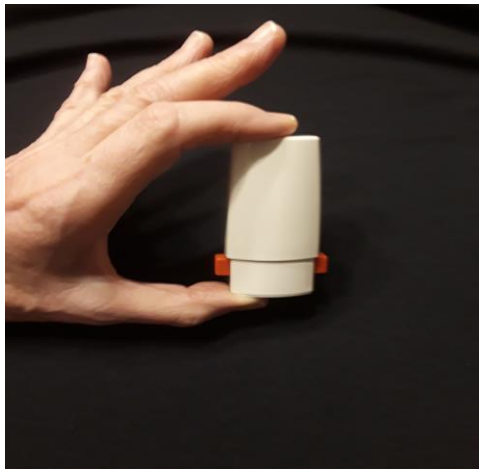
TEAEs at Month 2 in ≥4% of Patients Receiving LIQ861	Transitions				Add-Ons				Overall			
	No. (%) Subjects	No. of Events			No. (%) Subjects	No. of Events			No. (%) Subjects	No. of Events		
		Mld	Mod	Sev		Mld	Mod	Sev		Mld	Mod	Sev
Cough	**15 (27.3)**	14	1	0	**36 (54.5)**	29	7	0	**51 (42.1)**	43	8	0
Headache	**14 (25.5)**	12	2	0	**18 (27.3)**	13	4	1	**32 (26.4)**	25	6	1
Throat irritation	**5 (9.1)**	5	0	0	**14 (21.2)**	13	1	0	**19 (15.7)**	18	1	0
Dizziness	**6 (10.9)**	5	1	0	**7 (10.6)**	7	0	0	**13 (10.7)**	12	1	0
Diarrhea	**3 (5.5)**	2	1	0	**8 (12.1)**	5	3	0	**11 (9.1)**	7	4	0
Chest discomfort	**5 (9.1)**	4	1	0	**5 (7.6)**	4	1	0	**10 (8.3)**	8	2	0
Nausea	**4 (7.3)**	3	1	0	**5 (7.6)**	3	1	1	**9 (7.4)**	6	2	1
Flushing	**1 (1.8)**	1	0	0	**5 (7.6)**	5	0	0	**6 (5.0)**	6	0	0
Dyspnea	**3 (5.5)**	2	1	0	**3 (4.5)**	2	1	0	**6 (5.0)**	4	2	0
Oropharyngeal pain	**1 (1.8)**	1	0	0	**4 (6.1)**	4	0	0	**5 (4.1)**	5	0	0

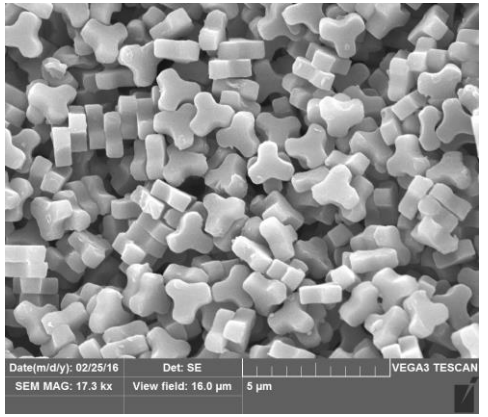
Source: data on file.

LIQ861 Met Primary Endpoint in Pivotal Phase 3 INSPIRE Study

A convenient, safe, well-tolerated option for inhaled prostacyclin therapy

- TEAEs consistent with known side effects of inhalation therapy (cough, throat irritation, and oropharyngeal pain) and prostacyclin (cough, headache, dizziness, diarrhea, chest discomfort, nausea, dyspnea, and flushing)
- Most TEAEs were mild to moderate in severity
- Eight subjects experienced TEAEs leading to study drug withdrawal or study discontinuation
- Five subjects experienced a serious TEAE, with none related to study drug
- Overall, 93% of patients remained on LIQ861 at Month 2





TEAE = treatment-emergent adverse event.
Source: data on file.

Thank You to Patients and Principal Investigators

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