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Safety and Tolerability of LIQ861 in Pulmonary Arterial Hypertension (PAH): Results From INSPIRE Study at 1 Year

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on behalf of the INSPIRE study investigators

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.

Research supported by Liquidia Technologies, Inc.

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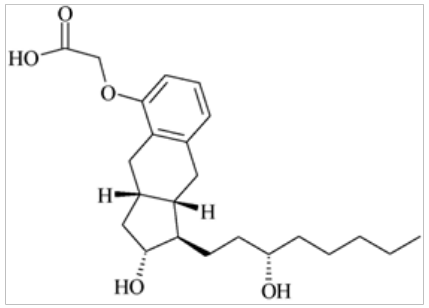
Tufts Medical Center

Liquidia

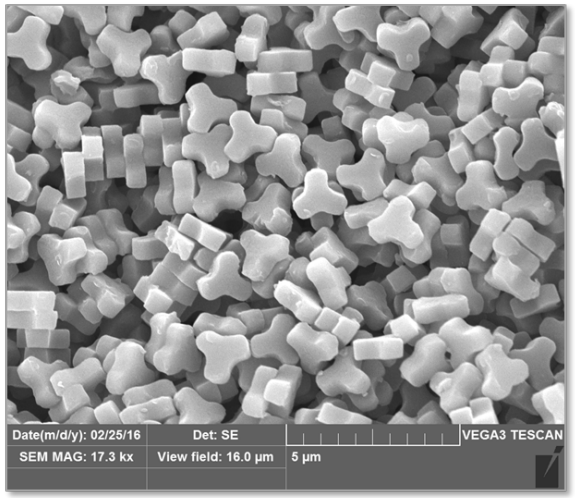
PRINT® Technology Results in a Uniform Size, Shape, and Chemical Composition of Dry Powder Inhalation Treprostinil Particles

Treprostinil



Treprostinil
(prostacyclin analog)

LIQ861 Dry-Powder Formulation



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®.

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EMEA, European Medicines Evaluation Agency; FDA, Food and Drug Administration; PK, pharmacokinetics.
Liquidia Technologies data on file. Tyvaso® is a registered trademark of United Therapeutics Corp.

INSPIRE Study Design

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

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AE, adverse event; NYHA, New York Heart Association; PCY, prostacyclin; Rx, prescription; SAE, serious adverse event.

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. Tyvaso® is a registered trademark of United Therapeutics Corp.

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%)

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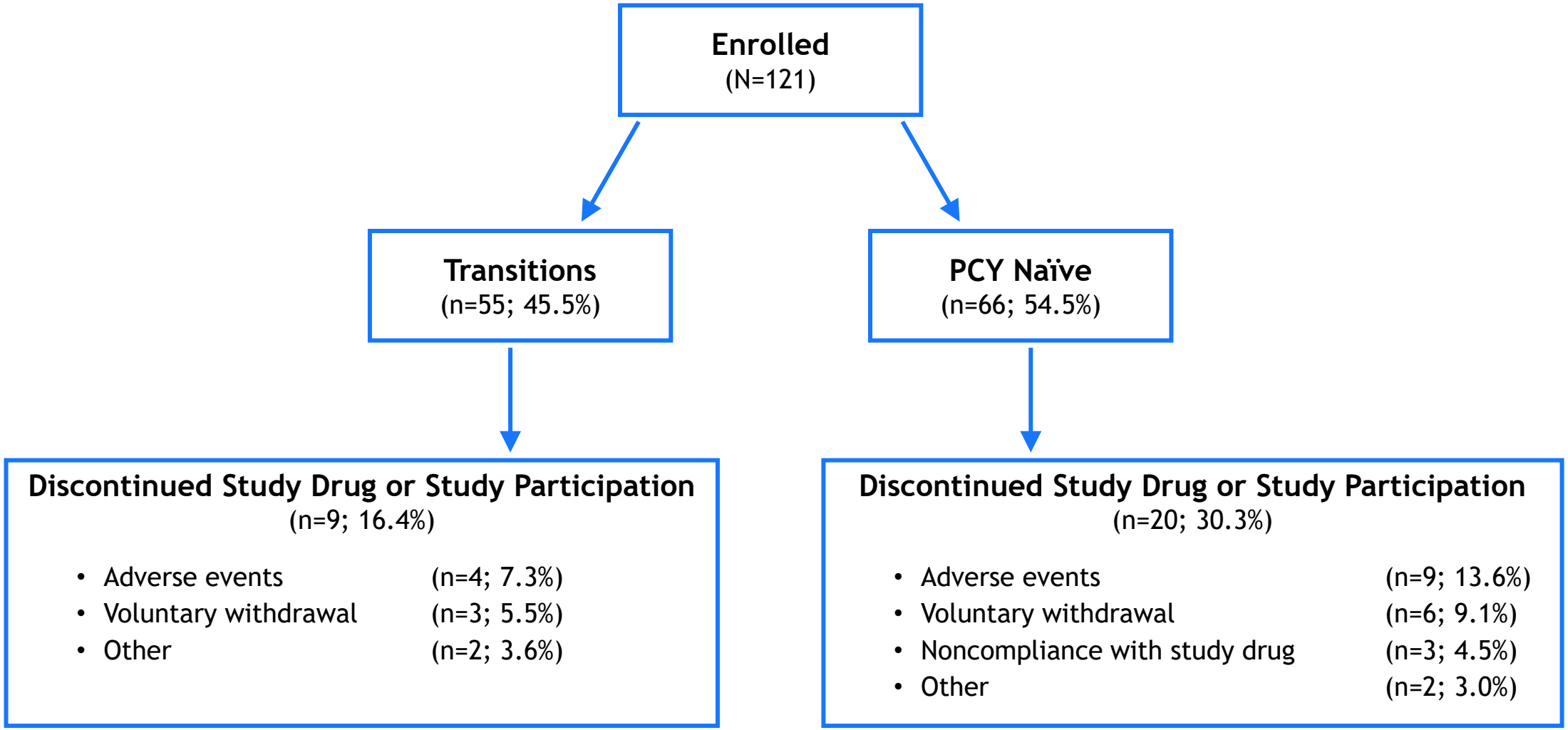
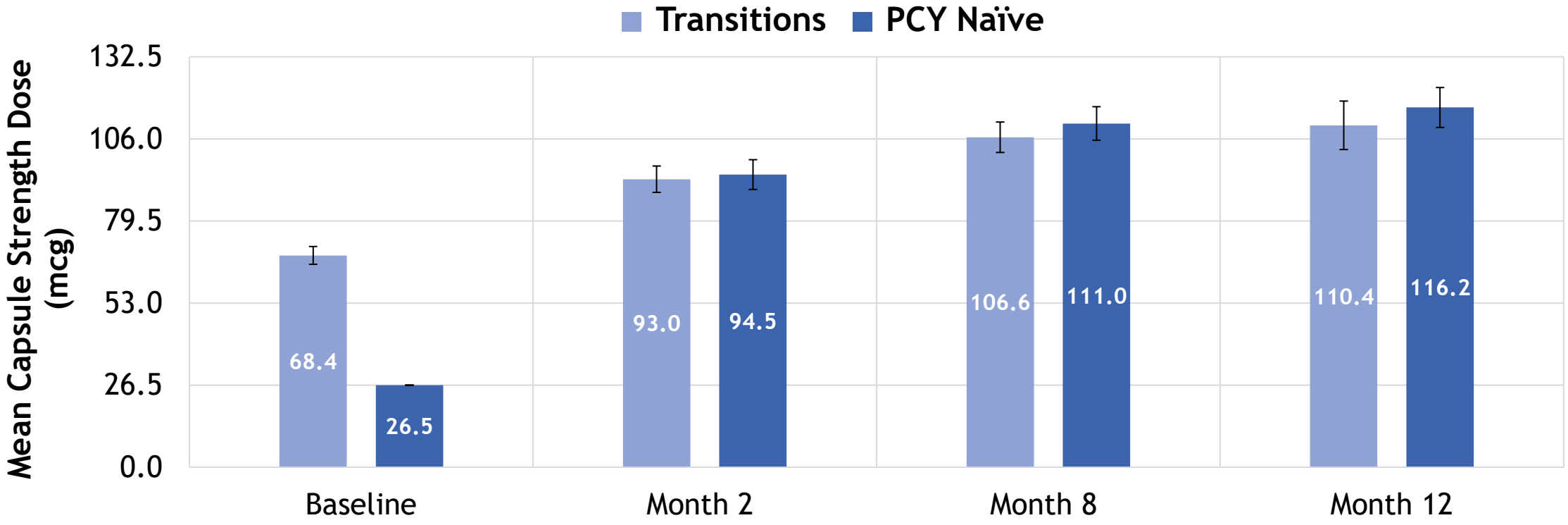
ERA, endothelin-1 receptor antagonist; PDE5i, phosphodiesterase type 5 inhibitor; PGI2, prostacyclin; SD, standard deviation; sGC, soluble guanylate cyclase stimulator.
Liquidia Technologies data on file.

Disposition of Patients



Liquidia Technologies data on file.

Patients Were Able to Increase the LIQ861 Dose During the Trial



- 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)

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QID, 4 times Daily.
Liquidia Technologies data on file.
Tyvaso® Is a Registered Trademark of United Therapeutics Corp.

AEs Related to Treatment Comprise the Majority of AEs and Are Commonly Seen with Inhaled Prostacyclin Therapy[1,2]

Most Common AEs (≥4%) Related to LIQ861 Treatment	Overall N=121			
	No. (%) Subjects	No. of Events		
		Mild	Moderate	Severe
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	1
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%).

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Liquidia Technologies data on file. 1. McLaughlin VV, Benza RL, Rubin LJ, et al. Addition of inhaled treprostinil to oral therapy for pulmonary arterial hypertension: a randomized controlled clinical trial. J Am Coll Cardiol. 2010;55(18):1915-1922. doi:10.1016/j.jacc.2010.01.027 2. Spikes LA, Bajwa AA, Burger CD, et al. BREEZE: Open-label clinical study to evaluate the safety and tolerability of treprostinil inhalation powder as Tyvaso DPI™ in patients with pulmonary arterial hypertension. Pulm Circ. 2022;12(2):e12063. Published 2022 Apr 7. doi:10.1002/pul2.12063

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		
		Mild	Moderate	Severe		Mild	Moderate	Severe
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

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Other Safety Data

- 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

SAE, Serious Adverse Event.
Liquidia Technologies data on file.

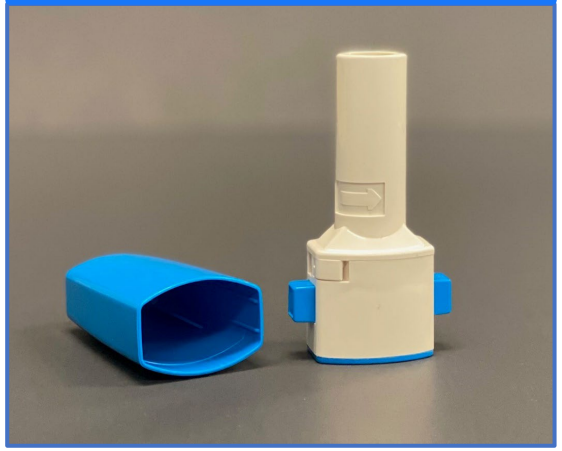
LIQ861 in Pivotal Phase 3 INSPIRE Study: Safety and Tolerability at 1 Year

- The study's primary objective was to evaluate the long-term safety and tolerability of LIQ861 through approximately one year of treatment with the option to roll over into an open-label extension.
- Other than expected prostanoid-related adverse events, inhaled administration of LIQ861 had no important adverse safety outcome during the INSPIRE trial.

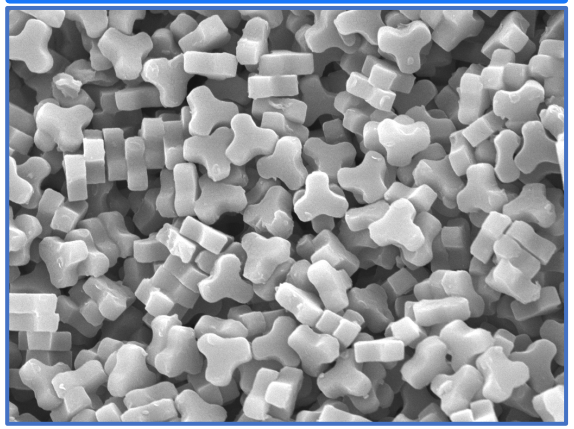
Clinical Implication

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

RS00 Model 8 Dry-Powder Inhaler



Dry Powder Treprostinil Developed Using PRINT



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Thank You to Patients and Principal Investigators

Roblee Allen, MD	University of California Davis
Hassan Alnuaimat, MD	University of Florida
David B. Badesch, MD	University of Colorado Denver
Remzi Bag, MD	University of Chicago
Charles Burger, MD	Mayo Clinic Jacksonville
Murali Chakinala, MD	Washington University School of Medicine, St. Louis
Shilpa DeSouza, MD	NYU Langone Hospital—Long Island
Hilary DuBrock, MD	Mayo Clinic
Jean Elwing, MD	UC Health
Jeremy Feldman, MD	Arizona Pulmonary Specialists, Ltd.
Micah Fisher, MD	Emory University
Jimmy Ford, MD	University of North Carolina Chapel Hill
Veronica Franco, MD	The Ohio State University
Nicholas Hill, MD	Tufts University School of Medicine
Akram Khan, MD	Oregon Health and Science University

Deborah Levine, MD	University of Texas Health Science Center San Antonio
Stacy Mandras, MD	Ochsner Clinic Foundation
John McConnell, MD	Kentuckiana Pulmonary Research Center, PLLC
Lana Melendres-Groves, MD	University of New Mexico Health Sciences Center
Ron Oudiz, MD	Los Angeles Biomedical Research Institute at Harbor UCLA Medical Center
Ioana Preston, MD	Tufts University School of Medicine
Marc Pritzker, MD	University of Minnesota
Amresh Raina, MD	Allegheny General Hospital
Stuart Rich, MD	Northwestern University
Rajeev Saggar, MD	Banner University Medical Research Institute
Sandeep Sahay, MD	Houston Methodist Research Institute
Trushil Shah, MD	The University of Texas Southwestern Medical Center
Shelley Shapiro, MD	VA Greater Los Angeles Healthcare System
Oksana Shlobin, MD	Inova Health Care Services
Marc Simon, MD	UPMC
Leslie Spikes, MD	University of Kansas Medical Center Research Institute
James Tarver, MD	Florida Hospital

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