TPIP Phase 2 PH-ILD Topline Results & Phase 2 PAH Blended Blinded Data Update

May 2024

Forward-Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. “Forward-looking statements,” as that term is defined in the Private Securities Litigation Reform Act of 1995, are statements that are not historical facts and involve a number of risks and uncertainties. Words herein such as “may,” “will,” “should,” “could,” “would,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “projects,” “predicts,” “intends,” “potential,” “continues,” and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) may identify forward-looking statements.

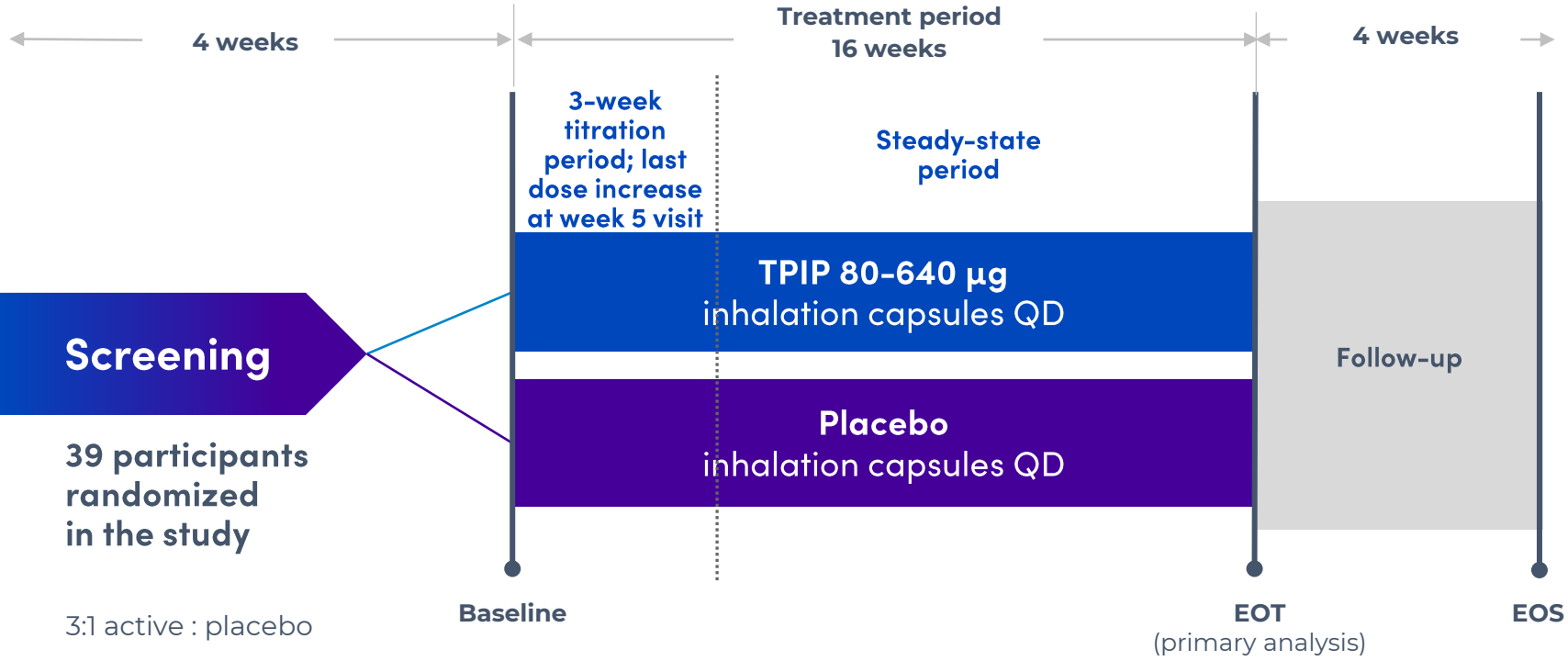
The forward-looking statements in this presentation are based upon the Company’s current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause the Company’s actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timings discussed, projected, anticipated or indicated in any forward-looking statements. Such risks, uncertainties and other factors include, among others, the following: development of unexpected safety or efficacy concerns related to treprostinil palmitil inhalation powder (TPIP) or our other product candidates; inaccuracies in our estimates of the size of the potential markets for TPIP or our other product candidates or in data we have used to identify physicians, expected rates of patient uptake, duration of expected treatment, or expected patient adherence or discontinuation rates; our inability to create or maintain an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of any of our product candidates that are approved in the future; risk that TPIP does not prove to be effective or safe for patients in ongoing and future clinical studies; risk that our competitors may obtain orphan drug exclusivity for a product that is essentially the same as a product we are developing for a particular indication; failure to successfully predict the time and cost of development, regulatory approval and commercialization for novel gene therapy products; failure to successfully conduct future clinical trials for TPIP and our other product candidates and our potential inability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval of our product candidates; risks that our clinical studies will be delayed, that serious side effects will be identified during drug development, or that any protocol amendments submitted will be rejected; risks that interim or partial data sets are not representative of a complete or larger data set or that blinded data will not be predictive of unblinded data; failure of third parties on which we are dependent to manufacture sufficient quantities of our product candidates for commercial or clinical needs, to conduct our clinical trials, or to comply with our agreements or laws and regulations that impact our business or agreements with us.

The Company may not actually achieve the results, plans, intentions or expectations indicated by the Company’s forward-looking statements because, by their nature, forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future. For additional information about the risks and uncertainties that may affect the Company’s business, please see the factors discussed in Item 1A, “Risk Factors,” in the Company’s Annual Report on Form 10-K for the year ended December 31, 2023 and any subsequent Company filings with the Securities and Exchange Commission (SEC).

The Company cautions readers not to place undue reliance on any such forward-looking statements, which speak only as of the date of this presentation. The Company disclaims any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

With respect to the blended and blinded data observed from the ongoing TPIP study in pulmonary arterial hypertension, the dose titration and efficacy analyses were based on data available as of April 1, 2024, and the safety analyses were based on data available as of January 25, 2024, respectively. These findings may not be representative of results after the study is completed and all data are collected and analyzed. As a result, later interim data readouts and final data from this study may be materially different than the observations described herein, including with respect to efficacy, safety and tolerability of TPIP.

TPIP Phase 2 PH-ILD Study Design & Endpoints



Green text indicates data disclosed on May 9, 2024

Primary Endpoints

- ***Safety and tolerability***
- ***Oxygenation***

Secondary Endpoints

Pharmacokinetics

Exploratory Efficacy Endpoints

- ***Improvement in 6-Minute Walk Distance (6MWD)***
- ***Improvement in biomarkers of cardiac stress (NT-proBNP)***
- Improvement in lung function and pulmonary vascular volume (FRI)
- Improvements in Quality of Life (CAMPHOR questionnaire)
- ***Clinical worsening****

* Clinical worsening is defined as one of the following: (1) Hospitalization due to a cardiopulmonary indication, (2) Lung transplantation, (3) Death from any cause, or (4) Decrease in 6MWD of at least 15% from baseline (at 2 consecutive visits at least 24 hours apart), directly related to disease.

TPIP Phase 2 PH-ILD Demographics and Baseline Characteristics

	Characteristics	TPIP QD (N=29)	Placebo (N=10)
Age, mean (SD)	**Age (years)**	65.7 (7.65)	63.8 (10.55)
Sex, % (n)	**Male**	69.0 (20)	80.0 (8)
	Female	31.0 (9)	20.0 (2)
Ethnicity, % (n)	**Hispanic or Latino**	24.1 (7)	20.0 (2)
Race, % (n)	**White**	82.8 (24)	90.0 (9)
	Multiple/ Not Reported	17.2 (5)	10.0 (1)
BMI, mean (SD)	**BMI (kg/m^2), (SD)**	26.82 (4.53)	26.08 (3.75)
Right Heart Catheterization, mean (SD)	**Cardiac Index**	2.53 (0.44)	2.39 (0.79)
	mPAP Mean Pulmonary Arterial Pressure, mmHg	34.3 (9.19)	33.6 (10.37)
	PVR Pulmonary Vascular Resistance, Wood Units	5.42 (2.06)	6.70 (3.05)
Pulmonary Function, mean (SD)	**FVC % pred**	57.5 (15.93)	64.2 (15.85)
	DLCO % pred	35.3 (11.16)	34.2 (19.61)
Supplemental Oxygen	**Supplemental Oxygen use (L/min)**	3.3 (2.17)	2.3 (2.16)

"N" = total participants randomized in specified group ; "n" = number of participants within the group

insmed

PH-ILD Phase 2 Study Met Primary Objective of Safety and Tolerability, With Lower Rates of Treatment Discontinuation and SAEs Compared to Placebo

Trial was randomized 3:1 TPIP vs. placebo

	TPIP (N=29)	Placebo (N=10)
Dose Titration % Patients Titrated to Maximum 640 µg Dose of TPIP or Placebo (n) % Patients Titrated to at least 480 µg Dose of TPIP or Placebo (n)	 79.3% (23) 89.6% (26)	 100.0% (10) 100.0% (10)
% Patients with Any TEAE (n)	93.1% (27)	90.0% (9)
% Patients with Study Drug Related[1] TEAE (n) % Patients with Study Drug Related Cough[2] (n)	55.2% (16) 37.9% (11)	40.0% (4) 0.0% (0)
% Patients with TEAE Leading to Treatment Discontinuation (n)	13.8% (4)	30.0% (3)
% Patients with Any SAE (n)	20.7% (6)	40.0% (4)
% Patients with Study Drug Related[1] SAE (n)	0.0% (0)	0.0% (0)
% Patient Deaths[3] (n)	6.9% (2)	20.0% (2)

"N" = total participants randomized in specified group ; "n" = number of participants within the group

[1] Based on investigator's evaluation. [2] All events of cough were mild, and none led to treatment discontinuation. [3] Includes any death that occurred on or after the first dose date. All deaths in the trial were related to disease progression or comorbid causes and none were attributed to TPIP.

TEAE=Treatment emergent adverse event SAE=Serious adverse event

No Meaningful Changes in Oxygen Saturation Levels Compared to Baseline for Patients Treated with TPIP

Trial was randomized 3:1 TPIP vs. placebo

	TPIP QD (N=29)		Placebo (N=10)	
	n	**Change from Baseline to Week 16**	***n***	**Change from Baseline to Week 16**
Supplemental Oxygen Use (L/min)	*24*	0.0 (0.91)	*8*	0.6 (2.20)
Pre-6MWT SpO_2 (%)	*24*	-0.3 (5.64)	*8*	-0.9 (3.04)
Lowest SpO_2 (%)	*22*	-4.6 (11.65)	*8*	-1.3 (7.03)
Post-6MWT SpO_2 (%)	*23*	-8.2 (14.07)	*8*	1.1 (4.45)

"N" = total participants randomized in specified group ; **"n"** = number of participants who reached Week 16
SpO_2 = Oxygen saturation **6MWT** = 6-minute walk test

insmed

Source: Table 16.2.8.5-1

Phase 2 PH-ILD Exploratory Efficacy Endpoints Support Advancement into Phase 3

Trial was randomized 3:1 TPIP vs. placebo

	TPIP (N=29)		Placebo (N=10)	
	Week 16	n	Week 16	n
6-Minute Walk Distance (6MWD) Treatment effect (TPIP vs. placebo) at Week 16[1] (m) Confidence interval P-value	30 [-49.0, 171.0] 0.3484	29	N/A	10
NT-proBNP concentrations (pg/mL)[2] (Baseline concentrations) Geometric mean ratio to Baseline (Geometric SD)	197.50 (242.90) 0.81 (3.36)	24	382.59 (338.43) 1.13 (1.50)	7
% Patients with Clinical Worsening Event (n) P-value (TPIP vs. placebo)[3]	10.3% (3) 0.0164	29	50.0% (5)[4]	10
% Patients hospitalized due to cardiopulmonary indication (n)	0.0% (0)	29	30.0% (3)	10
% Patients with decrease in 6MWD ≥ 15% from Baseline (n)	3.4% (1)	29	20.0% (2)	10
% Patients who died from any cause (n)	6.9% (2)	29	20.0% (2)	10

"N" = total participants randomized in specified group ; "n" = number of events, or participants within the group

[1]Calculation based on Hodges-Lehmann Estimate Location Shift [2]Calculation based on geometric mean [3]Calculation based on Fisher's Exact Test

[4]Two placebo patients each experienced two events, but this analysis counted only one event per subject.

Blended Blinded Phase 2 Data in PAH Indicates Potential of TPIP to Become Best-in-Class Prostanoid

	Blended/Blinded Data from Treatment and Placebo Arms (2:1 Randomization)
Dose Titration[1] Patients Titrated to Maximum Dose of 640 µg or Placebo (%)	**34 (79%)** of first 43 patients who reached Week 5 visit **Most countries have approved protocol changes to increase the maximum dose of TPIP from 640 µg to up to 1,280 µg, once daily, for the open-label extension of its PAH study**
Pulmonary Vascular Resistance (PVR)[2] Mean Reduction in PVR from Baseline	**19.9%** Based on first 40 patients who completed Week 16 of treatment, including active and placebo arms
6-Minute Walk Distance[3] Mean Improvement in Distance	**43 Meters** Based on first 40 patients who completed Week 16 of treatment, including active and placebo arms

2nd DMC meeting held in March 2024 recommended continuation of study as planned

[1]Dose titration analysis based on data available as of April 1, 2024. Dose titration data in PAH reflect first sets of patients in each trial who reached the Week 5 visit, which is the last possible point at which the dose can be increased in the trial.
[2]Efficacy analysis based on data available as of April 1, 2024. PVR data in PAH based on a review of 40 patients who had completed 16 weeks of treatment.
[3]6-Minute Walk Distance analysis based on data available as of April 1, 2024.
DMC = Data Monitoring Committee

insmed