Preliminary Baseline Data from the TETON Phase 3 Clinical Trials of Inhaled Treprostinil in the Treatment of Idiopathic Pulmonary Fibrosis

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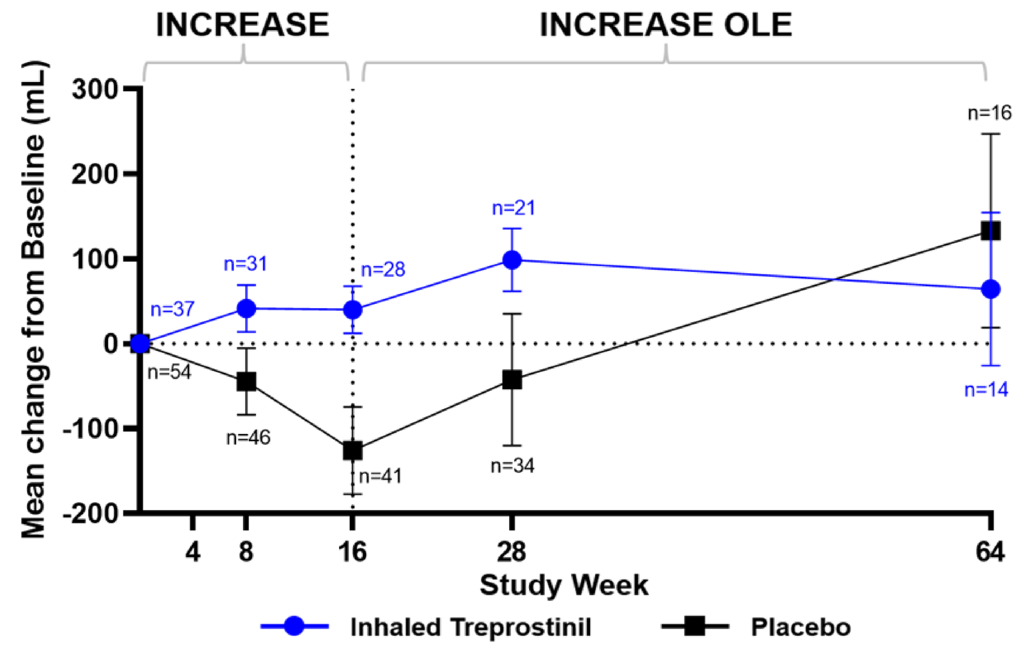
BACKGROUND

- Idiopathic pulmonary fibrosis (IPF) is a serious, chronic, progressive, fibrosing interstitial pneumonia with no known cause typically occurring in patients above 50 years of age.[1] It is characterized by progressive fibrosis and a radiological pattern known as usual interstitial pneumonia.[2] IPF greatly impacts quality of life and eventually leads to premature death from respiratory failure.
- In a post-hoc analysis of the landmark INCREASE study (NCT02630316) in patients with pulmonary hypertension due to interstitial lung disease, inhaled treprostinil demonstrated placebo-corrected improvements in forced vital capacity (FVC) and reduced exacerbations of underlying lung disease.[3,4] In subjects with IPF, between-treatment differences of 84.5 mL and 168.5 mL were observed in absolute FVC at Weeks 8 (p=0.11) and 16 (p=0.011), respectively (Figure 1).[4]
- Sustained improvements in FVC were also observed in the open-label extension study (INCREASE OLE, NCT02633293) for patients previously assigned to inhaled treprostinil. Marked improvements were observed when patients previously assigned to placebo switched over to inhaled treprostinil at Week 16 in the open-label extension (Figure 1).[5]
- These results, combined with preclinical evidence of treprostinil's antifibrotic activity, support its investigation in the treatment of IPF and led to the initiation of the TETON program (TETON-1/RIN-PF-301, NCT04708782; TETON-2/RIN-PF-303, NCT05255991).

Figure 1. Change from Baseline in Absolute FVC for IPF Subjects Enrolled in INCREASE and INCREASE OLE[5]



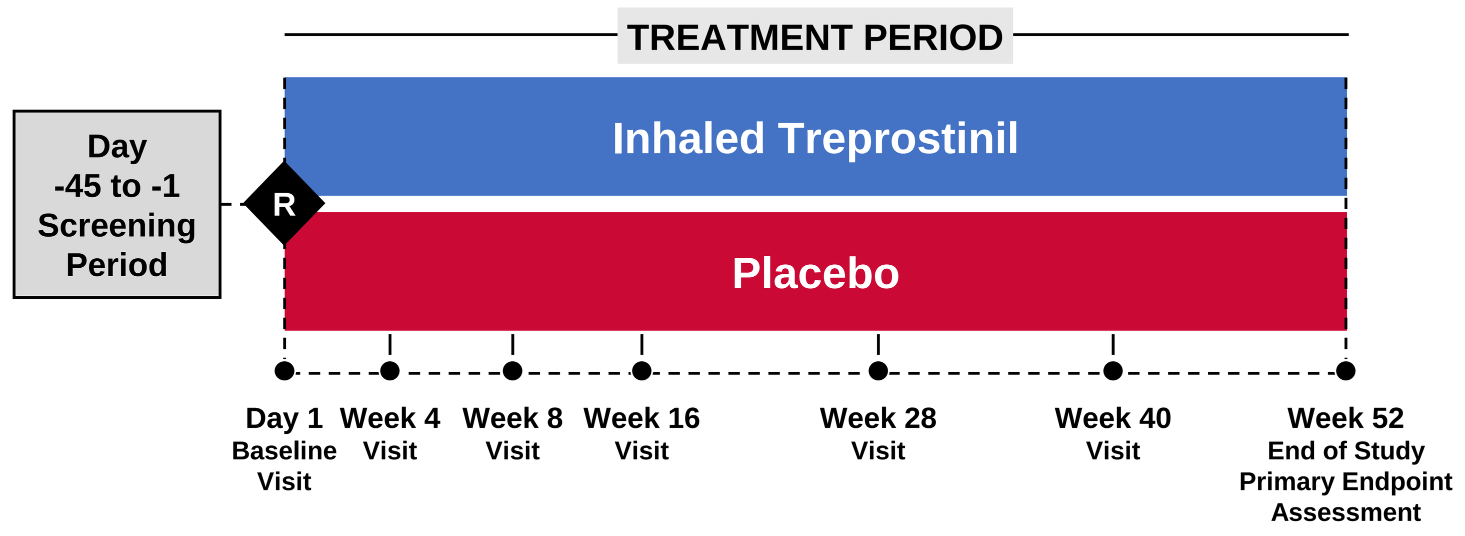
PHASE 3 OBJECTIVES/ENDPOINTS

- The primary objective of the TETON-1 and TETON-2 studies is to evaluate the safety and efficacy of inhaled treprostinil in patients with IPF. The primary efficacy endpoint is change in absolute FVC at Week 52. Secondary efficacy endpoints include time to clinical worsening (first event of death, respiratory hospitalization, or ≥10% decline in % predicted FVC), time to first acute exacerbation of IPF, overall survival, change in % predicted FVC, and change in the King's Brief Interstitial Lung Disease Questionnaire at Week 52.

METHODS

- The TETON program consists of two replicate, 52-week, randomized, double-blind, placebo-controlled, Phase 3 studies, each enrolling 396 subjects.
- Eligible patients must have a diagnosis of IPF confirmed by central imaging review, along with an FVC ≥45% predicted. Stable background use of pirfenidone or nintedanib is allowed.
- The studies consist of a Screening Period of up to 45 days and a 52-week Treatment Period. During the Treatment Period, 6 visits to the clinic are required at Weeks 4, 8, 16, 28, 40, and 52 (Figure 2).
- Safety parameters include adverse events, hospitalizations, oxygenation, and laboratory parameters.
- All subjects initiate inhaled treprostinil (6 mcg/breath) or placebo at a dose of 3 breaths (18 mcg) administered 4 times daily (QID; during waking hours) and titrate to a target dosing regimen of 12 breaths (72 mcg) QID.
- Patients who complete Week 52 on study drug will be eligible to enter an open-label extension study (TETON OLE/RIN-PF-302, NCT04905693).

Figure 2. Study Design of Studies TETON-1 and TETON-2



RESULTS (Data presented through April 1, 2023)

- Enrollment in the TETON studies is ongoing and anticipated to continue until target randomization in both trials has been reached. Sites are planned in approximately 19 countries globally (Figure 3).
- The data cut for this analysis includes a total of 265 subjects enrolled into both studies.
- Most subjects are male (77%) with a mean age of 72.1 years, and 3.8 years since IPF diagnosis. Subjects had mean baseline FVC of 2683 mL and mean % predicted FVC of 75%. Mean % predicted lung diffusion capacity (DLCO) at baseline was 52%. Approximately the same percentage of subjects were on nintedanib (40.8%) and pirfenidone (36.2%) background therapy (Table 1).
- Comparison of the baseline demographics for the TETON studies (Table 1) with the PH-IPF Population in the landmark INCREASE study (Table 2), which served as the basis for initiation of the TETON program, suggests that patients with IPF alone have higher FVC, higher DLCO, and lower supplemental oxygen use than subjects with concomitant PH.

RESULTS (Continued)

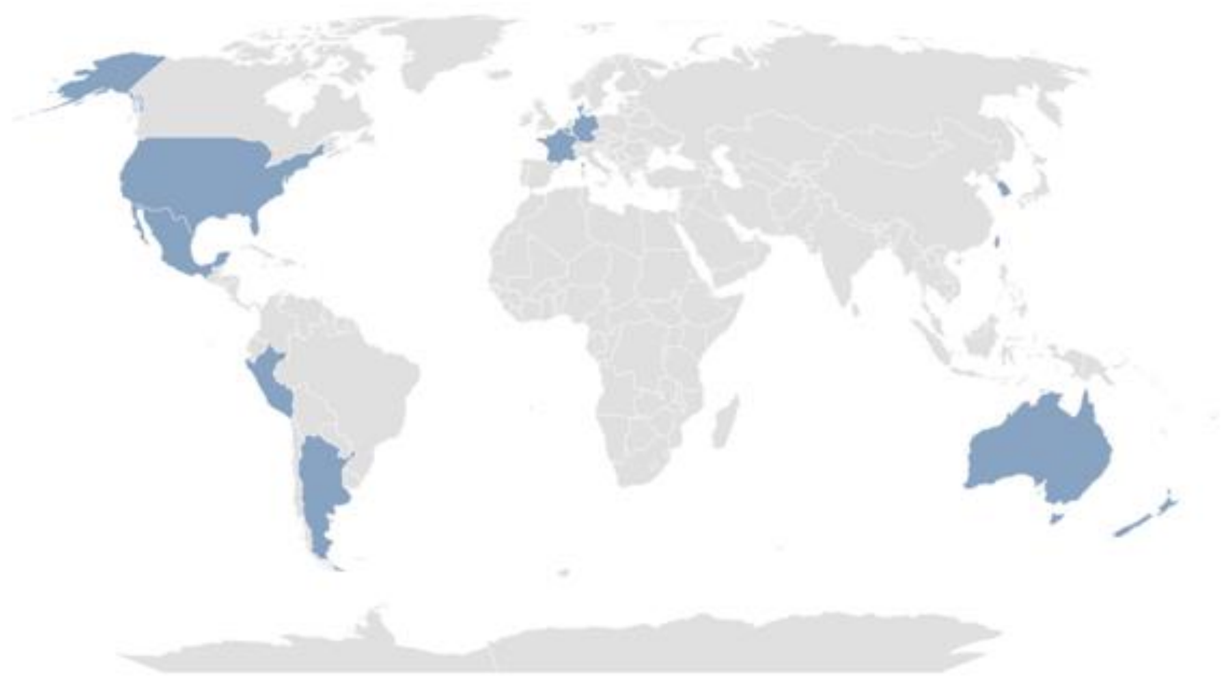
Table 1. Baseline Demographics: TETON-1 and TETON-2*

Age at Study Entry (years), mean (SD)	72.1 (6.9)
Female / Male	23% / 77%
Time Since IPF Diagnosis (years), mean (SD)	3.757 (2.831)
Ethnicity	
Hispanic or Latino	11%
Not Hispanic or Latino	86%
Not Reported	2%
Unknown	1%
Race	
White	91%
Asian	6%
American Indian or Alaska Native	0.8%
Black or African American	0.8%
Native Hawaiian/Pacific Islander	0.4%
Unknown	1.5%
FVC (mL), mean (SD)	2682.7 (692.4)
Percent Predicted FVC (%), mean (SD)	74.88 (19.21)
Percent Predicted DLCO (%), mean (SD)	51.53 (22.23)
FEV_1/FVC Ratio, mean (SD)	0.810 (0.061)
Use of Supplemental Oxygen	
No	80%
Yes	20%
Background Therapy	
Nintedanib	41%
Pirfenidone	36%
No background therapy	23%

Abbreviations: DLCO, lung diffusion capacity; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; IPF, idiopathic pulmonary fibrosis; SD, standard deviation

* = Results for the ongoing placebo-controlled blinded studies are presented for subjects overall.

Figure 3. TETON Program Country Selection



RESULTS (Continued)

Table 2. Baseline Demographics: INCREASE PH-IPF Population

Age at Study Entry (years), mean (SD)	70.8 (9.1)
Female / Male	34% / 66%
Ethnicity (%)	
Hispanic or Latino	11%
Not Hispanic or Latino	89%
Race (%)	
White	83%
Black	11%
Asian	4%
Native Hawaiian/Pacific Islander	2%
FVC (mL), mean (SD)	2192.1 (724.6)
Percent Predicted FVC (%), mean (SD)	60.8 (17.7)
Percent Predicted DLCO (%), mean (SD)	29.1 (11.5)
Use of Supplemental Oxygen	
No	26%
Yes	74%
Background Therapy	
Nintedanib	21%
Pirfenidone	33%
No background therapy	47%

Abbreviations: DLCO, lung diffusion capacity; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; IPF, idiopathic pulmonary fibrosis; PH, pulmonary hypertension; SD, standard deviation

CONCLUSIONS

- The prospectively designed TETON Phase 3 clinical trials aim to explore inhaled treprostinil for the treatment of IPF and may offer a much-needed inhaled treatment option for this vulnerable patient population.

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