Exploratory Efficacy Evaluation of PRM-151 in Patients With Idiopathic Pulmonary Fibrosis

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Background

- Dysfunctional wound repair upon injury appears to be central in the pathogenesis of Idiopathic Pulmonary Fibrosis (IPF).
- In response to tissue injury, monocytes can differentiate into Pro-inflammatory (M1) macrophages.
- Pro-fibrotic (M2) macrophages and fibrocytes.
- Regulatory (MREG) macrophages.

- Pentraxin-2 binds to monocyte Fc-γ-receptors and promotes their differentiation into regulatory macrophages, promoting resolution of fibrosis.
- Prevents differentiation into M2 pro-fibrotic macrophages and fibrocytes, preventing fibrosis.
- PRM-151, or recombinant human Pentraxin-2, is in development for fibrinous diseases, including IPF.

Preclinical

Pentraxin-2 and PRM-151 reduce fibrosis in preclinical models of lung fibrosis

- PTX-2 decreases collagen and improves lung function in the rat bleomycin model.

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Objectives

- Safety and tolerability of multiple, ascending, intravenous doses of PRM-151 in patients with IPF.
- PK and PD profile of multiple IV doses of PRM-151 in patients with IPF.
- Prospective, randomized, double-blind, placebo-controlled, with multiple dose administrations of: Placebo or PRM-151 at 1, 5 or 10 mg/kg in successive patient cohorts.
- IV administration on days 1, 3, 5, 8 and 15.

Phase I Study Schedule

Mean change from baseline to Day 57

FVC (L/min) -4.0 (1.5) -4.0 (1.5) 0.19

DLC0 (absolute change in %) -4.2 (4.2) -4.2 (4.2) 0.19

Relative change from baseline to Day 57

Individual Patient Data

FVC % Predicted

- For all exploratory efficacy endpoints - in subjects with ≥35% FVC % relative change from baseline

PRM-151 treatment at all doses showed a trend towards improvement of pulmonary function (FVC and DLC0) at 8 weeks.

Patients with the greatest improvements in FVC had improvement in additional exploratory efficacy endpoints.

Endogenous Pentraxin-2 is indistinguishable from PRM-151, so PRM-151 levels were calculated by subtracting baseline Pentraxin-2 levels from values at all subsequent timepoints.

Cmax and AUC are dose proportional from 1 to 10 mg/kg; Mean t½ is 32.8 hrs.

No detectable anti-drug antibodies on Day 29 or Day 57.

PRM-151 does not accumulate when administered on a weekly basis.

PRM-151 was well tolerated in this typical population of older, sick patients with IPF.

No Serious Adverse Events and no severe adverse reactions.

No dose limiting toxicity.

No infusion reactions.

Conclusions

- PRM-151 administered 5 times over 15 days, was well tolerated at 1, 5 and 10 mg/kg in patients with IPF.
- PRM-151 treatment at all doses showed a trend towards improvement of pulmonary function (FVC and DLC0) at 8 weeks.
- Patients with the greatest improvements in FVC had improvement in additional exploratory efficacy endpoints.
- These data support Phase 2 investigation of PRM-151 in IPF.