

# PBI-4050 Reduces Inflammatory/Fibrotic Markers in a Bleomycin-Induced Lung Fibrosis Model: a Comparative Study with Nintedanib



PROMETIC

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## INTRODUCTION

The pathological mechanisms underlying the development of idiopathic pulmonary fibrosis (IPF) are highly complex. PBI-4050, a novel first-in-class orally active low molecular weight compound, plays a key role in inflammation/fibrosis regulation by reducing profibrotic cytokines, fibrocyte differentiation, myofibroblast activation and EMT, resulting in improvement of organ function.

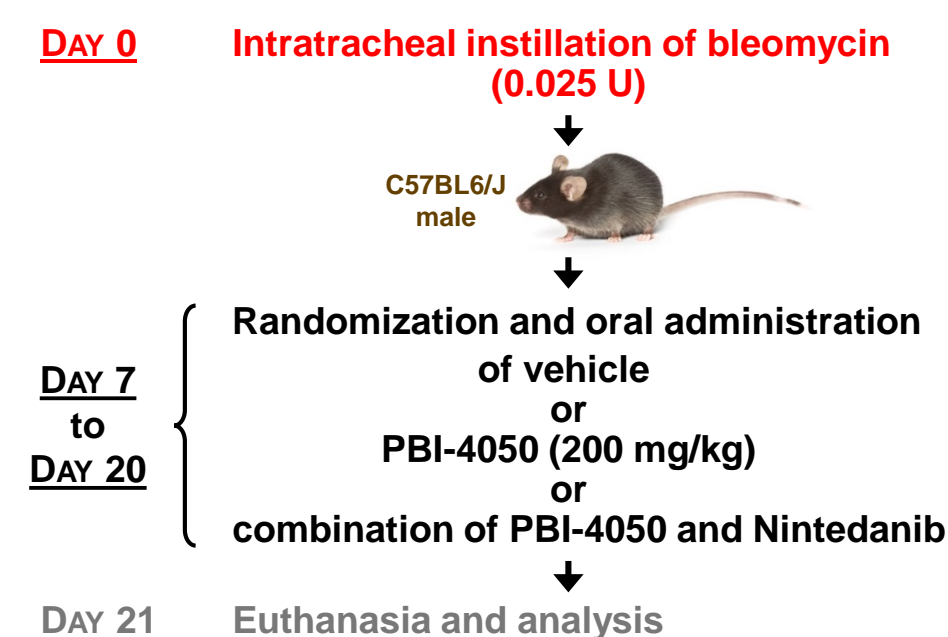
The aim of this study is to compare the anti-fibrotic activity of PBI-4050, or combination of PBI-4050 and Nintedanib (BIBF), in the bleomycin-induced lung fibrosis model.

## STUDY DESIGN

Mice were randomized according to their bleomycin-induced body weight loss, and treatments with PBI-4050 or combination of BIBF and PBI-4050 started on day 7. Only animals that recovered their body weight loss by day 20 were used for data analysis.

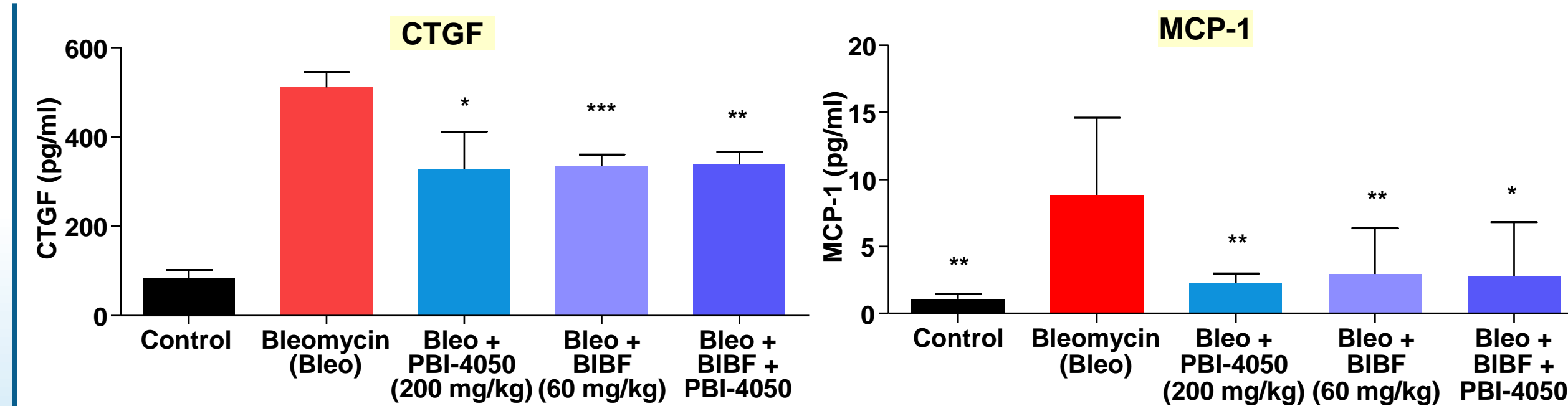
\* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .

### MODEL OF BLEOMYCIN-INDUCED PULMONARY FIBROSIS

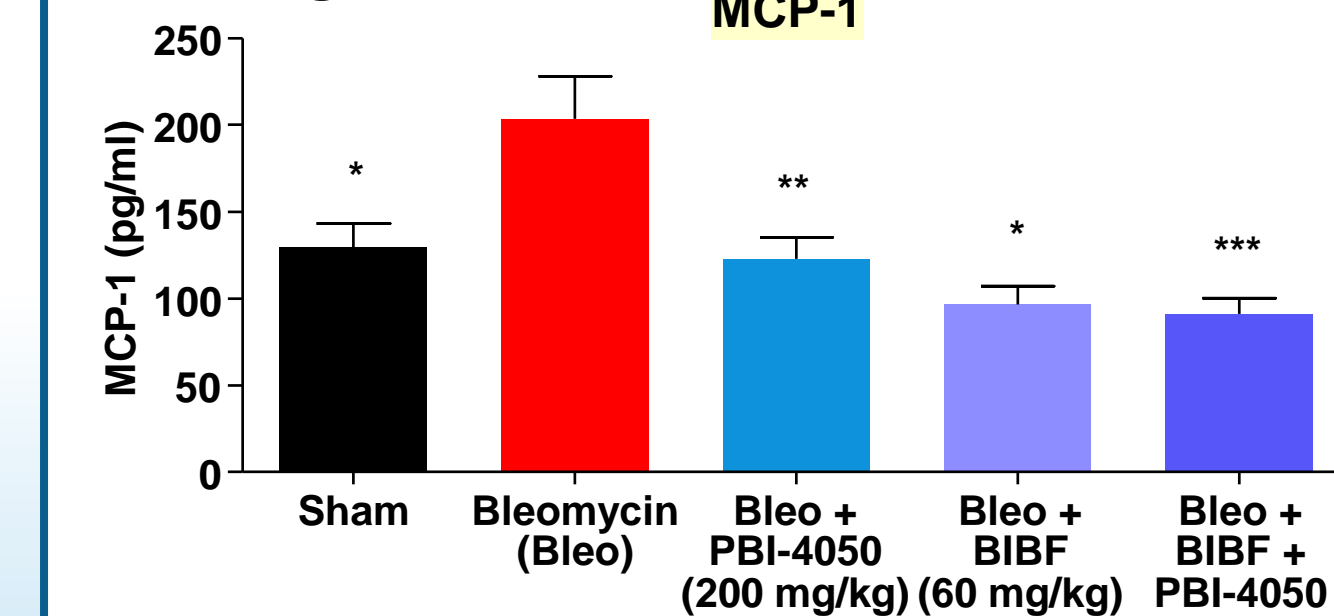


## RESULTS

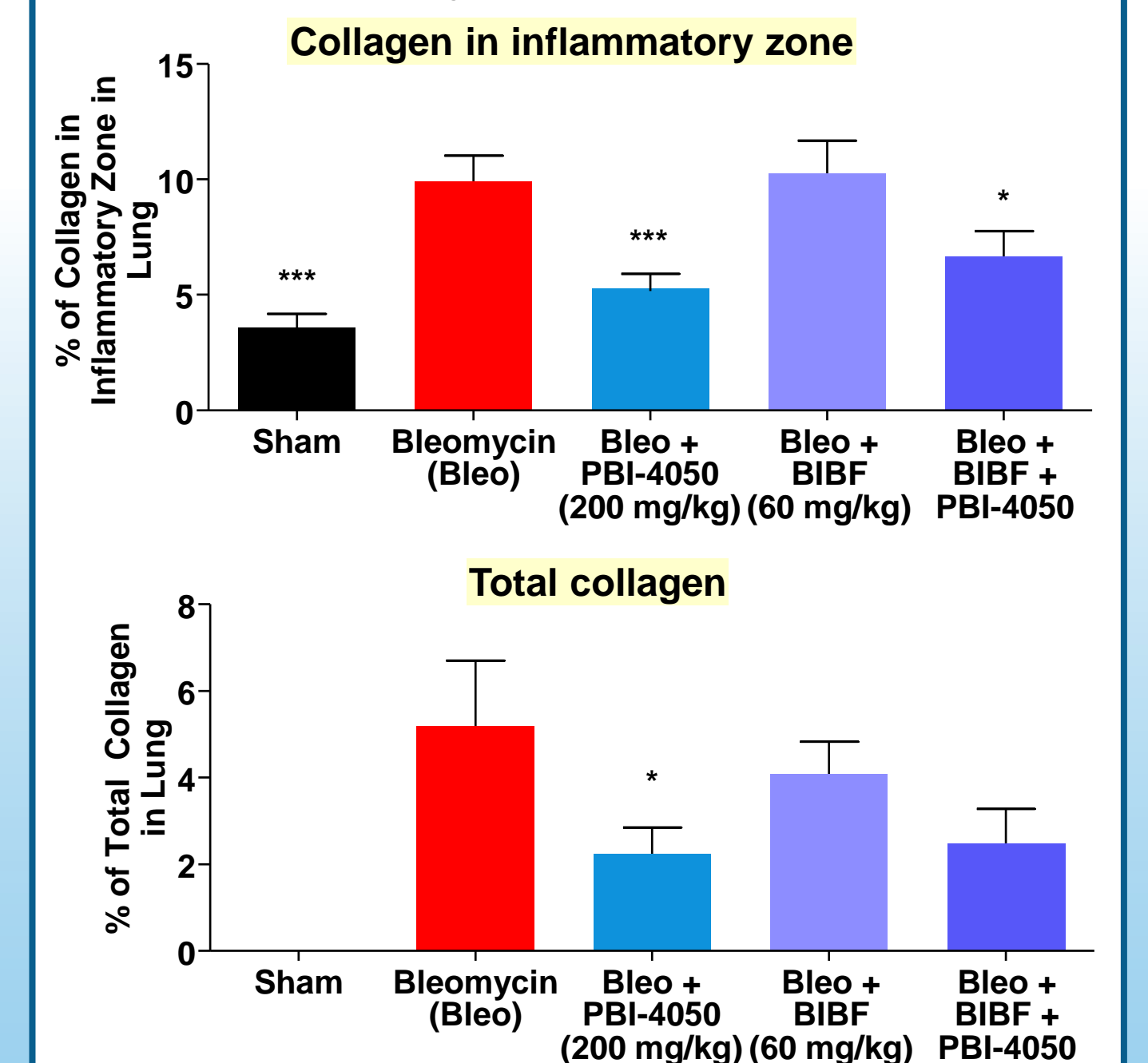
**A** Effect of treatment regimen on MCP-1 and CTGF level in BALF



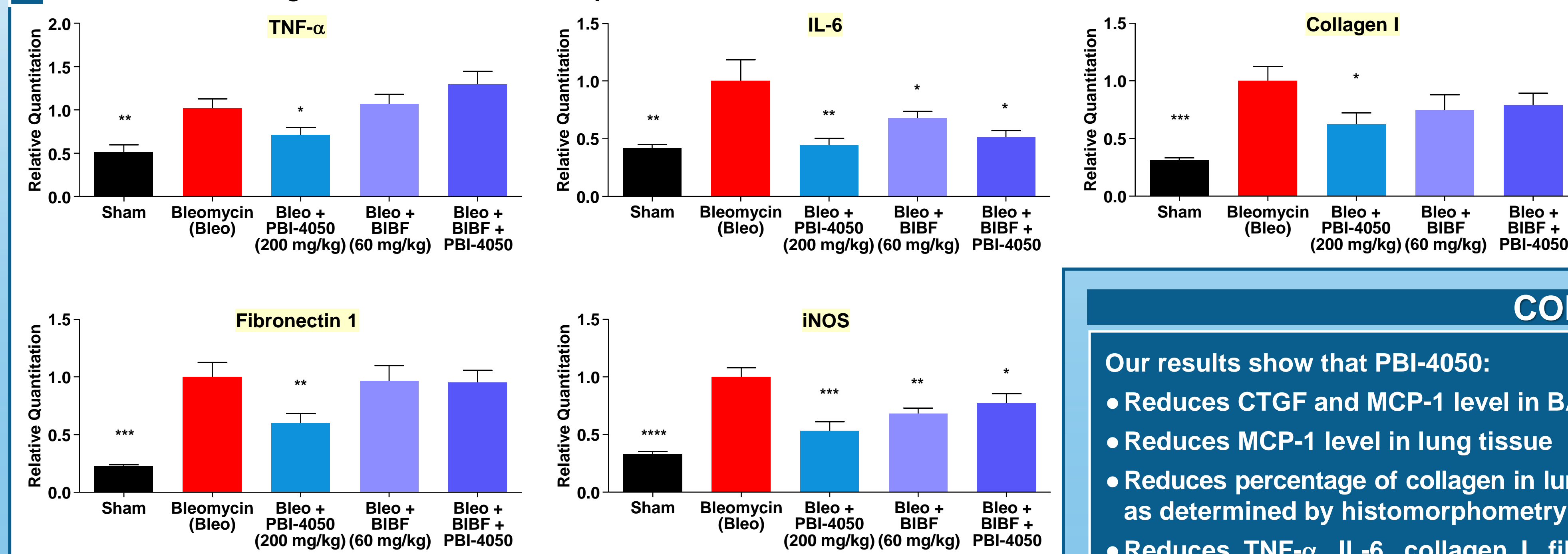
**B** Effect of treatment regimen on MCP-1 level in lung tissue



**C** Effect of treatment regimen on collagen in inflamed lung area determined by histomorphometric analysis



**D** Effect of treatment regimen on fibrotic marker expression



## CONCLUSION

Our results show that PBI-4050:

- Reduces CTGF and MCP-1 level in BALF
- Reduces MCP-1 level in lung tissue
- Reduces percentage of collagen in lung tissue, as determined by histomorphometry
- Reduces TNF- $\alpha$ , IL-6, collagen I, fibronectin and iNOS mRNA expression in lung tissue

PBI-4050 may be an efficacious treatment in IPF. The combination therapy with Nintedanib provides no superior outcomes.