FIRST REPORT MANAGED CARE

Advancing Value in IPF Management With Nerandomilast

Results From the FIBRONEER-IPF Extended Follow-Up Study

Background

- IPF is a chronic lung disease characterized by inflammation and fibrosis of the lung interstitium. Disease progression is inevitable, but current treatment options suffer from burdensome toxicity profiles, limiting their long-term utility.[1, 2]
- Nerandomilast offers a novel mechanism of action, as a selective PDE4B inhibitor, targeting key fibrotic and inflammatory pathways to attenuate disease progression in IPF.[3]
- The FIBRONEER-IPF extended follow-up results demonstrate the efficacy and safety of nerandomilast up to 76 weeks, including in patients receiving background therapy with nintedanib and pirfenidone.[4]

Abbreviations

AE = adverse event

DL_{CO} = diffusing capacity (of lung) for carbon monoxide

FVC = forced vital capacity

IPF = interstitial pulmonary fibrosis

ILD = interstitial lung disease

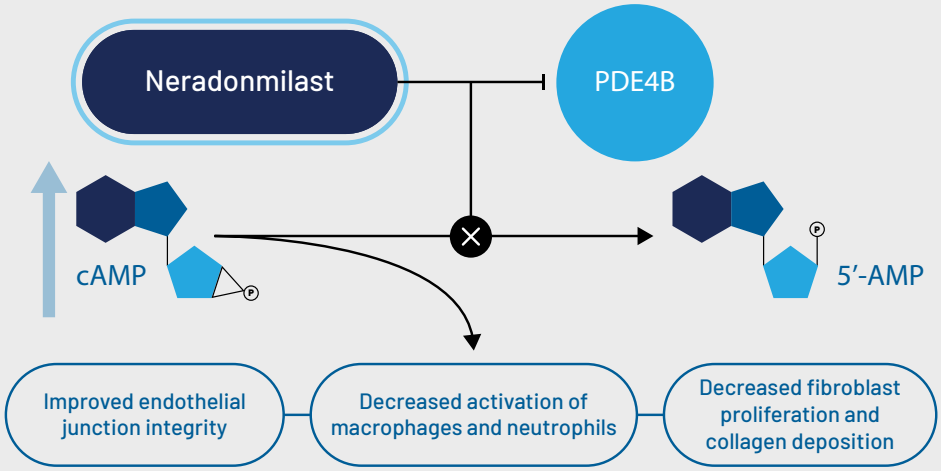
MOA = mechanism of action

PDE = phosphodiesterase

UIP = usual interstitial pneumonia

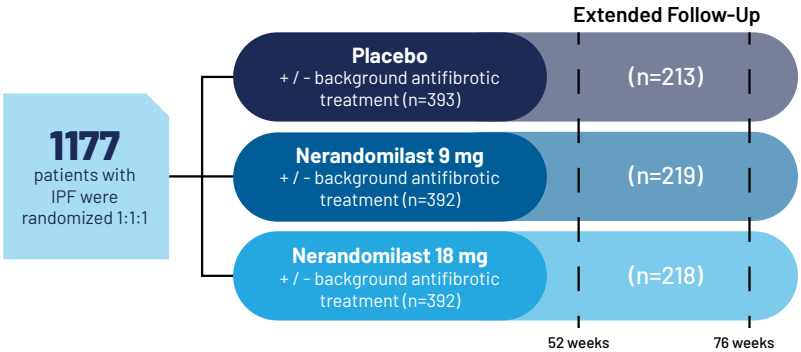
Nerandomilast offers a novel MOA that inhibits profibrotic and inflammatory pathways[5]

1. Nerandomilast preferentially inhibits PDE4B over other PDE4 isoforms.
2. PDE4B inhibition suppresses the degradation of cAMP to 5′-AMP, leading to intracellular cAMP accumulation.
3. Reduced 5′-AMP leads to reduced expression of profibrotic growth factors and inflammatory cytokines.



FIBRONEER-IPF Trial With Extended Follow-Up[6]

- FIBRONEER-IPF met its primary endpoint: at 52 weeks, patients receiving either dose of nerandomilast saw a significantly smaller decline in their FVC compared to placebo.
- Nerandomilast exhibited a tolerable safety profile, with diarrhea being the most common adverse reaction.
- Treatment discontinuation rates were low among patients receiving nerandomilast compared to placebo.

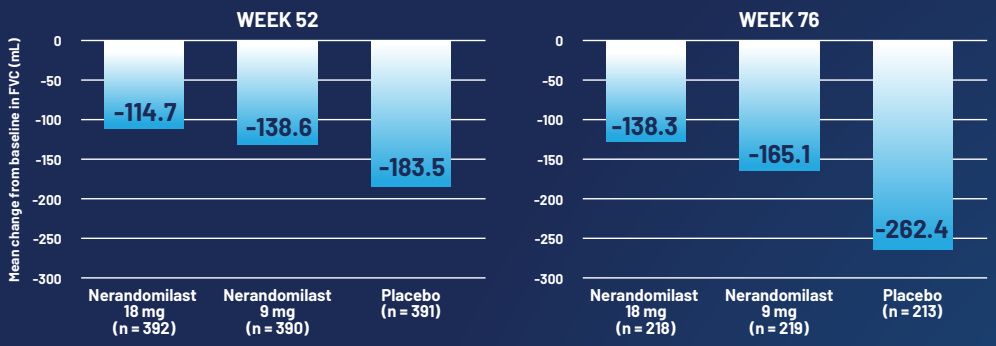


Primary endpoint:
Absolute change from baseline in FVC at 52 weeks

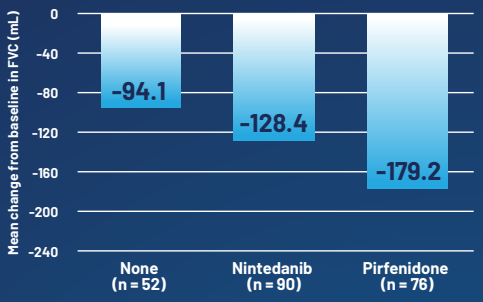
Secondary endpoint:
A first acute exacerbation, hospitalization for a respiratory cause, or death

Sustained Disease-Modifying Effects Through Week 76

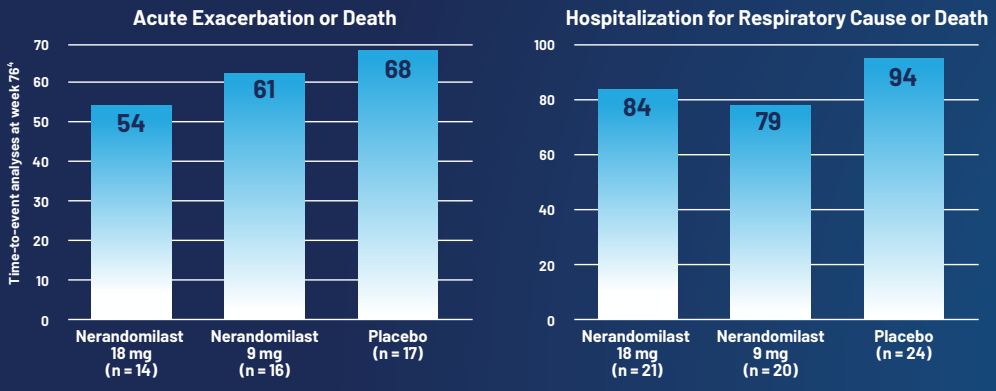
Reduction in FVC decline at week 52 was sustained through week 76.[4, 6]



Reduction in FVC decline was observed in the presence or absence of background therapy.[4]



Treatment with nerandomilast led to numerically fewer acute exacerbations or death, as well as hospitalizations due to respiratory cause or death, compared to placebo at week 76.[4]



Consistent Safety Profile Through Week 76[4]

- Nerandomilast demonstrated a safety profile consistent with prior findings, with serious adverse events balanced across groups and no new safety signals identified.
- Overall discontinuation rates due to adverse events were comparable across treatment arms, though higher rates were observed among patients receiving background nintedanib.

Treatment Discontinuation Due to Adverse Events at Week 76

No background therapy		
12.6% Placebo	**10.2%** 9 mg Nerandomilast	**9.2%** 18 mg Nerandomilast
Nintedanib		
13.9% Placebo	**18.5%** 9 mg Nerandomilast	**23.0%** 18 mg Nerandomilast
Pirfenidone		
12.0% Placebo	**8.3%** 9 mg Nerandomilast	**23.0%** 18 mg Nerandomilast

Study Limitations[4]

- The relatively short follow-up period limited the number of events, particularly deaths, which constrained the ability to fully assess long-term outcomes like mortality.
- Acute exacerbations and respiratory hospitalizations were not formally adjudicated, which may introduce variability or uncertainty in outcome reporting.
- Small subgroup sizes and a known drug-drug interaction with pirfenidone may limit interpretation of efficacy in certain populations. Additionally, analyses were not adjusted for multiple testing.

Economic Impact

- By slowing progression and improving persistence, nerandomilast may help delay advanced disease, preserve function, and reduce downstream health care utilization.
- The flexibility to use nerandomilast as a monotherapy or add-on therapy supports individualized treatment approaches and broader clinical use.
- The FIBRONEER-IPF extended follow-up data supports nerandomilast's value across efficacy, safety, and adherence, adding to the therapeutic landscape of IPF.

References

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3. Reininger D, Wolf F, Mayr CH, et al. Insights into the cellular and molecular mechanisms behind the antifibrotic effects of nerandomilast. *Am J Respir Cell Mol Biol*. 2025;73(5):700-712. doi:10.1165/rcmb.2024-0614OC.
4. Oldham JM, Azuma A, Kreuter M, et al. Nerandomilast in idiopathic pulmonary fibrosis: data from the whole follow-up period of the FIBRONEER-IPF trial. *Am J Respir Crit Care Med*. Published online February 21, 2026. doi:10.1093/ajrccm/aamag058.
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6. Richeldi L, Azuma A, Cottin V, et al. Nerandomilast in patients with idiopathic pulmonary fibrosis. *N Engl J Med*. 2025. doi:10.1056/NEJMoa2414108.