ASPIRE, a global, double-blind, randomized, placebo-controlled Phase 2b trial of buloxibutid, an angiotensin II type 2 receptor agonist, in idiopathic pulmonary fibrosis: trial design and patient characteristics

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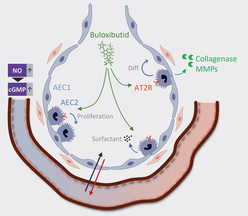
Background and Rationale

- Idiopathic pulmonary fibrosis (IPF) is a severe, progressive respiratory disease. Despite available antifibrotics, high morbidity is still a major burden, reflecting the need for new therapies.
- Buloxibutid is an oral small molecule angiotensin II type 2 receptor (AT2R) agonist, designed to target the AT2R on alveolar epithelial type 2 (AEC2) cells and believed to initiate downstream anti-fibrotic, anti-inflammatory, and tissue-reparative signaling pathways.
- In a Phase 2a clinical trial (the AIR trial), treatment with buloxibutid was associated with stabilized and improved forced vital capacity (FVC) over 36 weeks, warranting further investigation into the safety and efficacy of buloxibutid in IPF.
- ASPIRE is an ongoing randomized, placebo-controlled Phase 2b trial that is designed to assess the efficacy and safety of two doses of buloxibutid over 52 weeks in patients with IPF.
- Here, we present the ASPIRE trial design and patient characteristics.

Buloxibutid is an Oral Small Molecule AT2R Agonist Designed to Support Tissue Repair Through Alveolar Epithelial Type 2 cells (AEC2)

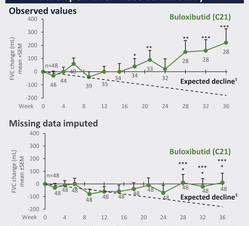
Buloxibutid is designed to target AT2R on AEC2[1,2]



Buloxibutid: Expected effects in IPF[1,2]

- **Increased AEC2 viability** and surfactant production
- **Reduced** TGF-β1 production, EMT, and collagen accumulation
- **Anti-remodeling** and vasodilatation (NO release)

Stabilization and improvement of FVC in the open label Phase 2a AIR study [3–5]



‡ Expected average decline of 180 mL/36 weeks for untreated patients based on published placebo data.[4,5]
*p<0.05, **p<0.01, ***p<0.001, t-test versus expected untreated decline.
n=48 patients with 2-week FVC change from baseline data.

AEC2: alveolar epithelial type 2 cell; AT2R: angiotensin II Type 2 receptor; C21: compound 21; cGMP: cyclic guanosine monophosphate; EMT: epithelial-mesenchymal transition; FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; MMP: matrix metalloproteases; NO: nitric oxide; SEM: standard error of the mean; TGF-β1: transforming growth factor beta 1.

ASPIRE is a Global Trial Representing a Broad IPF Patient Population

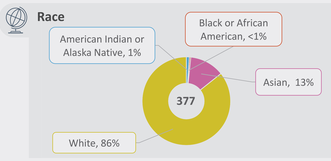
Characteristics, N=377*

21.8% female
78.2% male

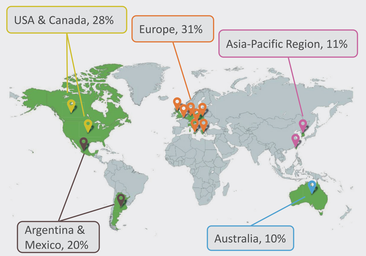
Mean (SD) age at study entry: **71.1** (7.5) years

Mean (SD) BMI: **27.9** (4.8) kg/m²

Race



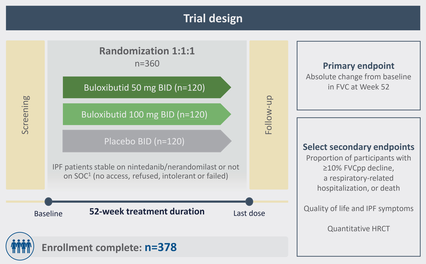
> 100 study sites across 14 countries



BMI, body mass index; SD, standard deviation. *Total randomized participants exposed to at least one dose of IMP. Preliminary data, reflecting 16 June 2026 database extract.

The ASPIRE Trial in Patients with IPF was Designed to Assess Changes in FVC over 52 Weeks

Trial design



Primary endpoint
Absolute change from baseline in FVC at Week 52

Select secondary endpoints
Proportion of participants with ≥10% FVCpp decline, a respiratory-related hospitalization, or death

Quality of life and IPF symptoms

Quantitative HRCT

Enrollment complete: **n=378**

Key inclusion and exclusion criteria

- Age ≥ 40 years
- Diagnosed with IPF within the last 7 years
- FVC ≥ 50% predicted
- DLCO ≥ 30% predicted
- UIP – prob. UIP on HRCT scan < 36 months
- Stable dose of approved IPF therapy

- Treatment with pirfenidone within 8 weeks
- FEV_1/FVC ratio <0.7
- Heart failure NYHA Class IV
- PH with syncopal episode
- Acute IPF exacerbation within 3 months

AV: atrioventricular; BID: twice daily, DLCO: diffusing capacity of the lungs for carbon monoxide; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; FVCpp: FVC percent predicted; HRCT: high-resolution computed tomography; IPF: idiopathic pulmonary fibrosis; NYHA: New York Heart Association; PH: pulmonary hypertension; QTcF: corrected QT interval; SOC: standard of care; UIP: usual interstitial pneumonia.

ASPIRE Baseline Patient Data are Reflective of a Typical Cohort of Patients with IPF

Time since diagnosis
2.4 (1.7) years

Smoking status

36.9% never smoked
61.5% former smokers
1.6% current smokers

FVC, mean (SD)
2.9 L (0.8)

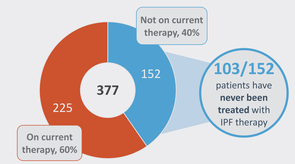
FVCpp, mean (SD)
81.3% (17.6)

FEV_1/FVC ratio, mean (SD)
0.8 (0.06)

DLCOpp, Hb corrected, mean (SD)
54.1% (15.7)

Oxygen saturation, mean (min – max)
96.0% (86% – 100%)

Previous and current IPF therapy at study entry



DLCO: diffusing capacity of the lungs for carbon monoxide; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; FVCpp: FVC percent predicted; Hb: haemoglobin; HRCT: high-resolution computed tomography; IPF: idiopathic pulmonary fibrosis; SD: standard deviation. Preliminary data, reflecting 16 June 2026 database extract.

Conclusions

- Buloxibutid is an **angiotensin II type 2 receptor agonist** designed to support tissue repair through alveolar epithelial type 2 cells
- ASPIRE is an ongoing randomized, placebo-controlled Phase 2b study that is designed to assess the efficacy and safety of **two doses of buloxibutid over 52 weeks** in patients with IPF
- Patients enrolled in ASPIRE are **generally representative of the IPF population**, with a mean time since diagnosis of 2.4 years and 40% of participants not receiving background therapy
- The global distribution of enrolled participants demonstrates that ASPIRE successfully captured a **geographically diverse IPF population**, supporting the relevance and applicability of the study across regions

References

[1] Steckelings UM, et al. Pharmacol Rev 2022; 74:1051–135; [2] Nalbandyan A et al. FASEB 2018; 32(S1):829.7; [3] Vicore data on file. ;
[4] Noble PW et al. Eur Respir J 2016; 47: 243–53; [5] Richeldi L et al. N Engl J Med 2014; 370:2071–82.

Conflicts of Interest Disclosure: Toby Maher

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vicore pharma