

ASPIRE – crafting a patient-focused 52 week phase 2b trial of buloxibutid (C21), an oral angiotensin II type 2 receptor agonist, in patients with IPF



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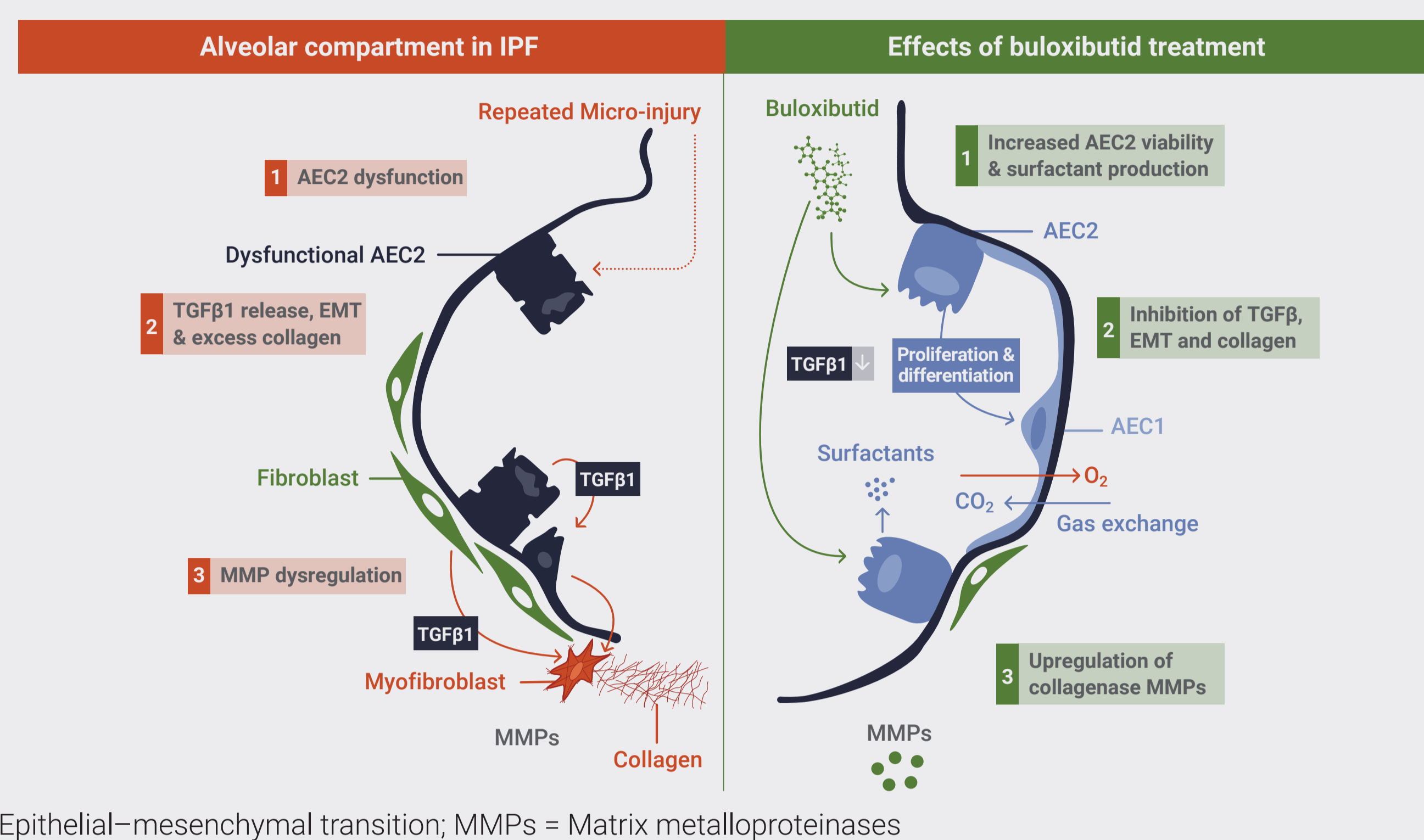
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Background and rationale

The unmet medical need in idiopathic pulmonary fibrosis (IPF) remains monumental with multiple trials failing to demonstrate efficacy. Additionally, many clinical trials fail to recruit enough participants or suffer high dropout rates, increasing the hurdles for developing new and effective therapies.¹

Buloxibutid (C21) is a novel oral, selective angiotensin II type 2 (AT2) receptor agonist with disease modifying potential in IPF. Buloxibutid drives an upstream pathway to improve alveolar epithelial type 2 cell (AEC2) function, triggering a cascade of anti-fibrotic activity, and resolving disease-associated vascular remodeling.

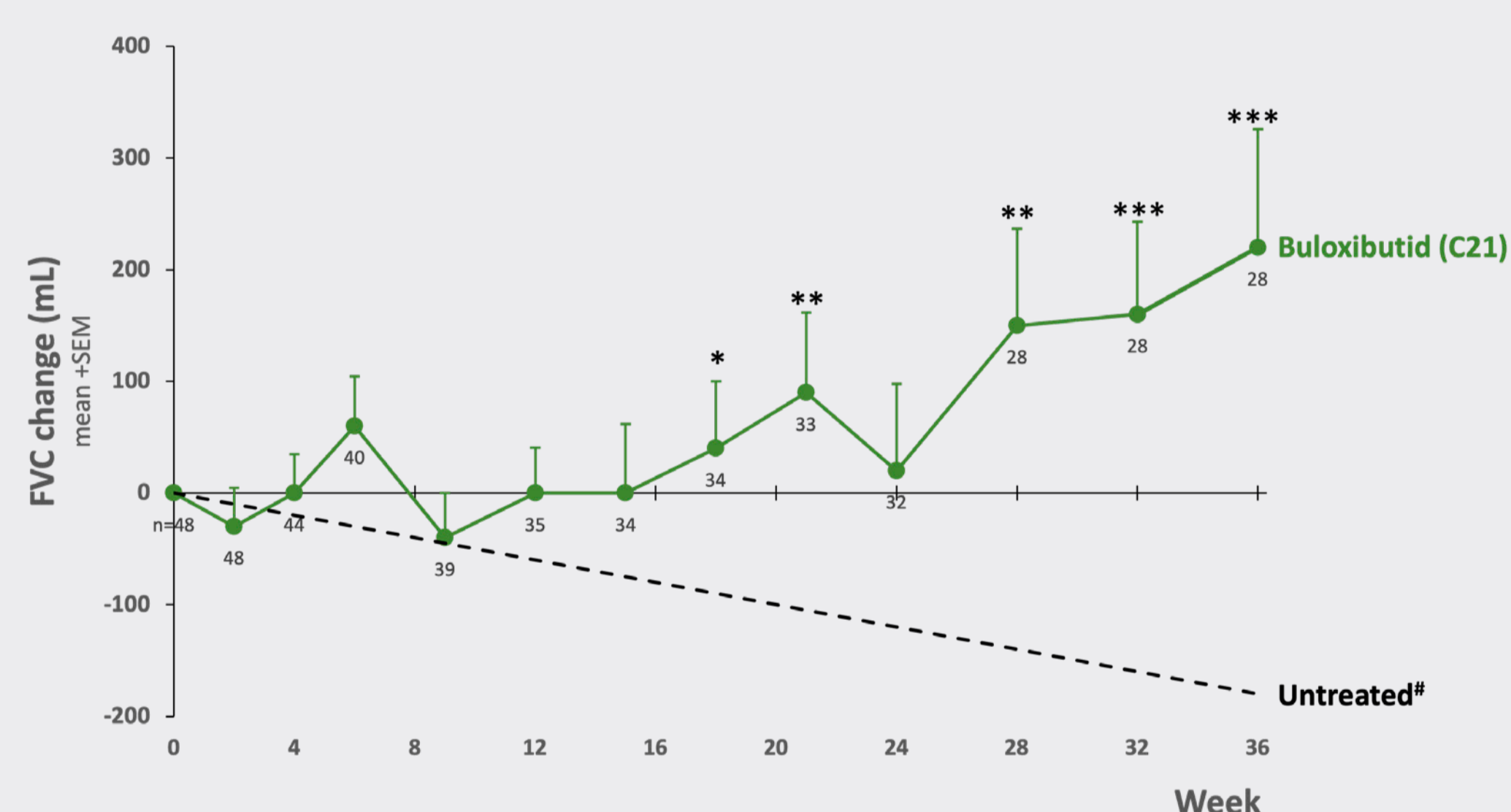
Buloxibutid - disease modifying potential



Buloxibutid stabilized and improved lung function over 36 weeks in the phase 2a AIR trial. The safety profile showed excellent gastrointestinal tolerability and no treatment related serious adverse events.

Learning from the AIR trial and recent publications, Vicore recognizes that to meet patients' needs and priorities, and to ensure that trial participation is attractive and convenient, increased patient involvement in trial design and set-up is required.^{2,5}

Final results of the 36 week IPF interventional AIR trial²

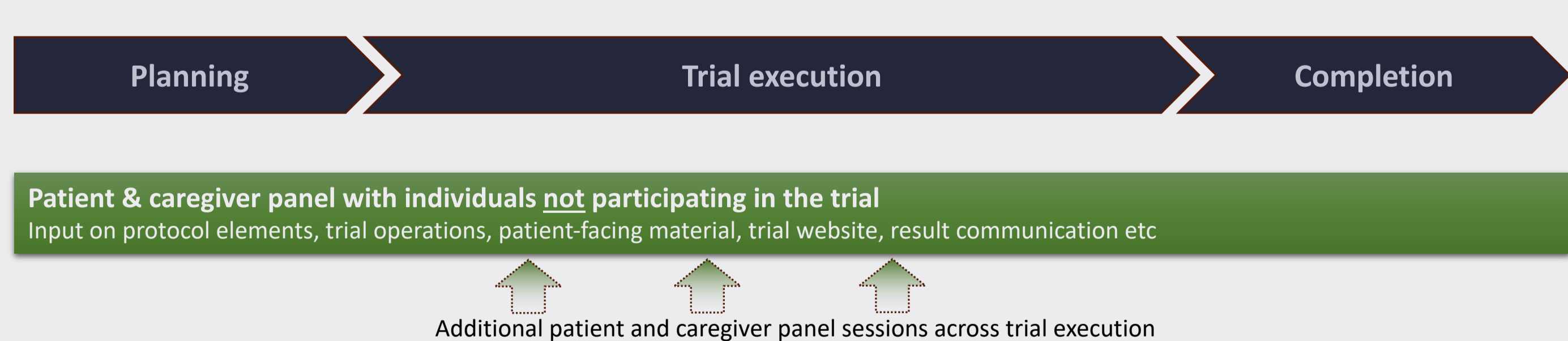


Note: n=48 patients with 2-week FVC data. Observed values, no imputation.
Untreated: Expected average decline for untreated patients based on published placebo data^{3,4}
*p<0.05, **p<0.01, ***p<0.001; t-test versus expected untreated decline corresponding to -120 mL/24 weeks

Methods

In ASPIRE, a planned 52-week, randomized, double-blind, placebo-controlled, phase 2b trial of buloxibutid, early patient involvement was secured by the establishment of an advisory panel consisting of six patients and two caregivers from the United Kingdom and the United States. Patients in the panel will not be included as participants in the ASPIRE trial. The first interaction included a two-hour, semi-structured panel discussion followed by five individual interview sessions. Qualitative feedback was sought on the participants' clinical research experience and the ASPIRE trial protocol and patient-facing materials. Several interactions are planned during the conduct of the trial.

Aspiring to bring patient and caregiver voices into the trial



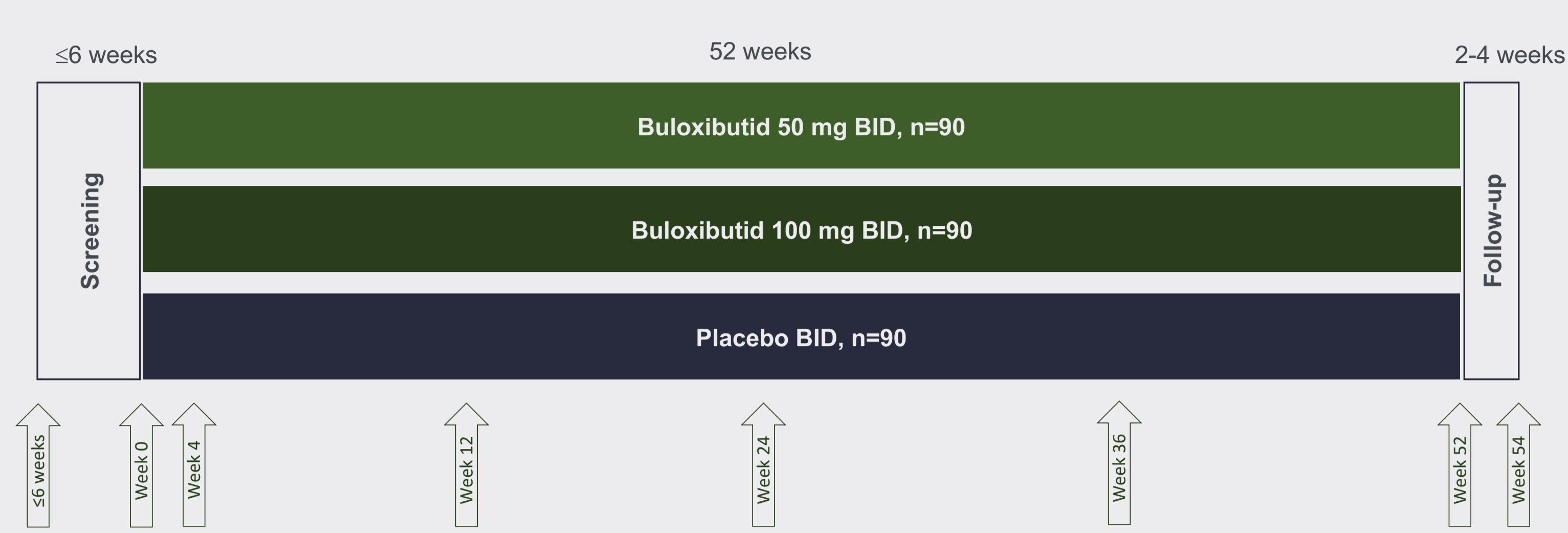
Results

The six patient panellists were 61-80 years of age, predominantly males (83%), with a time since diagnosis of 0-5 years. All were on approved IPF therapy and 50% had previous clinical trial experience. The two caregiver panellists were 71-80 years of age and females. The feedback from the first interaction fell into three main categories: patient first, patient feedback, and promises fulfilled – the “3 PFs”.

In the ASPIRE trial, patients on nintedanib standard-of-care may continue on therapy in the trial and a 2:1 allocation to buloxibutid versus placebo increases the chance of receiving active treatment. Trial visits are partly decentralized, i.e., several visits are conducted as phone or video call from patients' home and on-site visit frequency is kept to a minimum. Patient-involvement activity will be published to enable sharing of experiences and learnings.

ASPIRE trial design – a total of 8 site visits and 8 remote visits

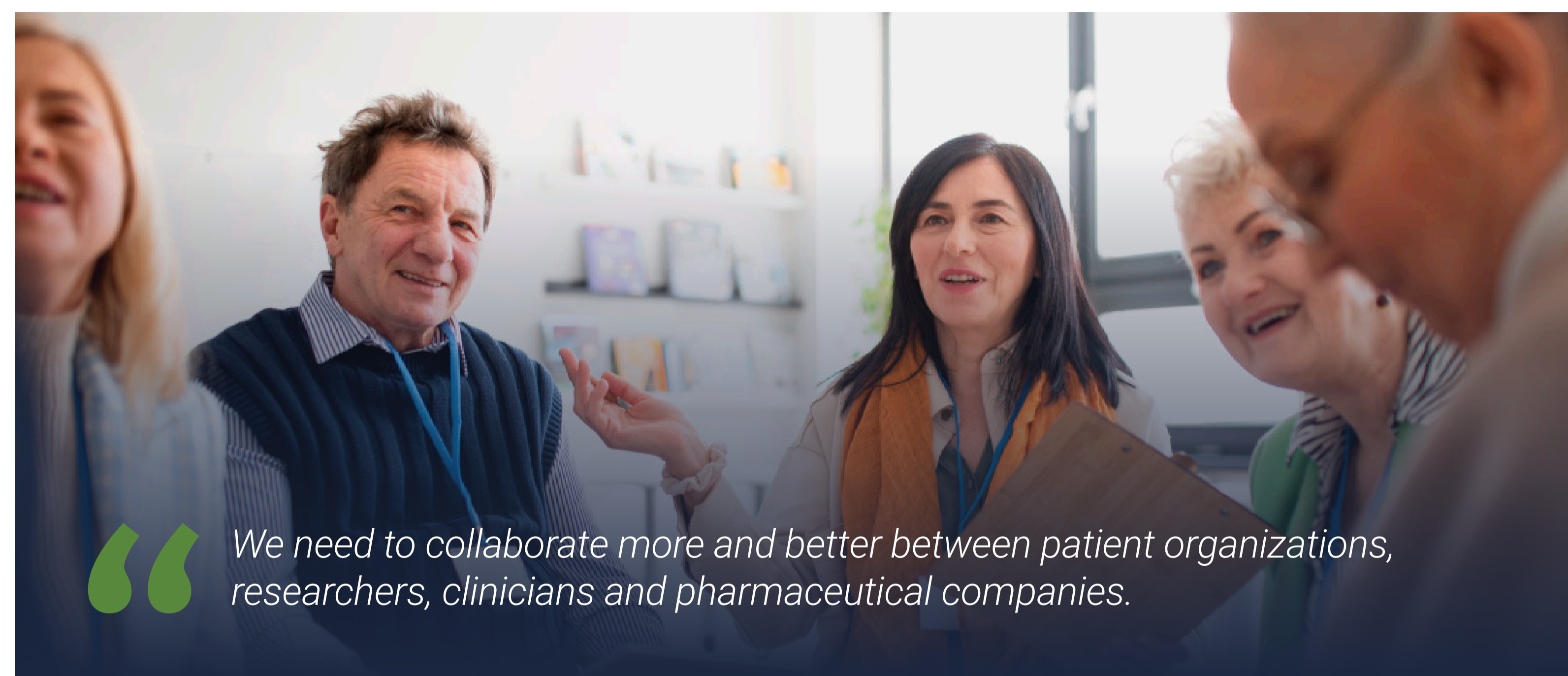
270 Subjects with Idiopathic Pulmonary Fibrosis Randomized 1:1:1



The “3 PFs” and qualitative feedback*

- Patient First** Importance of **understandable, comprehensive and transparent trial communication to trial participants and caregivers**, including trial design, procedures, potential benefits, side effects and individual trial progress. Consider **trial participant and caregiver needs and preferences** including compensation and support services, visit schedule flexibility, home-based monitoring and efficient coordination at trial sites to minimize waiting times.
- Patient Feedback** Importance of **collecting qualitative and quantitative patient feedback** throughout trial planning, conduct and reporting. Use **multiple sources** for patient feedback e.g., through patient organizations and support networks, trial-specific panels and trial participants.
- Promises Fulfilled** **Being able to fulfill promises** is a key motivation for trial retention and further engagement. **Realistic expectation management** can be achieved by including patients and caregivers in the process.

* Documented qualitative feedback collected during the first patient and caregiver panel interaction for ASPIRE.



Discussion

Involvement of patients and caregivers in the design of clinical trials has been strongly advocated and is also encouraged in the International Council For Harmonisation (ICH) guidelines. Active involvement of people affected by a disease will likely increase trust in the trial, facilitate enrollment and promote adherence, since they have valuable insights into whether scheduled procedures may be overly burdensome and lead to early dropouts.⁶ The importance of anchoring IPF trial endpoints on real patient experiences - namely, how they feel, function, and survive - has also been highlighted by a range of clinical trial stakeholders (patients, investigators, and regulatory representatives).⁷



Conclusions

- ⊙ IPF patients need access to new improved treatments which requires scientifically rigorous trials that are patient centric.
- ⊙ ASPIRE aims for success through continuously listening to patients and caregivers with an ambition to increase trial participant empowerment.
- ⊙ Vicore is in the forefront by committing the “3 PFs” to guide the design, conduct and reporting of the ASPIRE trial.