## SUPPLEMENTARY METHODS

**Cohort.** To qualify for INSPIRE, patients had to be diagnosed with IPF within 48 months of randomization by surgical biopsy and/or by existing radiological criteria applied to a mandatory baseline high-resolution computed tomography (HRCT) scan. The HRCT criteria for definite IPF included the presence of reticular abnormalities, traction bronchiectasis, or both, with a basal and peripheral predominance; honeycombing with a basal and peripheral predominance; and the absence of atypical features of usual interstitial pneumonia (UIP). Probable IPF was defined by a bilateral, predominantly basal and subpleural reticular pattern with subpleural cysts (honeycombing), traction bronchiectasis, or both, in the absence of atypical features. Of note, the classification of IPF has changed since the time of this trial and no longer includes a "possible" category (2). Additional enrollment criteria included the requirement that clinical symptoms be present for at least 3 months, with evidence of disease progression in the prior 12 months. Mandated Pulmonary Function Test (PFT) parameters included a forced vital capacity (FVC) of 55–90% of the predicted value, a hemoglobin-corrected carbon monoxide diffusing capacity ($DL_{CO}$) of 35–90% of the predicted value, and a 6-minute walk distance (6MWD) of at least 150 meters. In all patients younger than 50 years with a clinical and radiological diagnosis of "probable IPF", surgical lung biopsy samples were required, regardless of the certainty with which the clinical and radiological diagnoses were made. Importantly, the study protocol did not specify a fixed number of follow-up chest CT scans during the trial; therefore, the frequency of subsequent chest CT scans (performed based on clinical indications) was not standardized across all participants. The steering committee did support the development of a biobank of serological specimens collected during study visits, which became available for investigator-initiated studies after the trial's conclusion. However, the trial did not include long-term follow-up of participants.

**IP-to-MS.** A data-dependent acquisition with parallel accumulation-serial fragmentation (DDA-PASEF) method was utilized to generate mass spectrometric data, which were then searched

with MaxQuant (version 2.1.3.0) against a reviewed human protein database from Uniprot (downloaded on 6/10/2024).