

# INTEGRIS-IPF Phase 2a Trial Week 24 Analysis of Bexotegrast 320 mg Cohort

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#### **Today's Speakers**







Bernard Coulie, M.D., Ph.D. President & CEO Éric Lefebvre, M.D. Chief Medical Officer Greg Cosgrove, M.D., FCCP Vice President, Clinical Development



Toby Maher, M.D., Ph.D. Director of ILD, Keck School of Medicine, USC





# Bernard Coulie, M.D., Ph.D. President and Chief Executive Officer

#### **INTEGRIS-IPF** – Introduction

#### Purpose of Evaluating Long-Term Treatment with Bexotegrast 320 mg

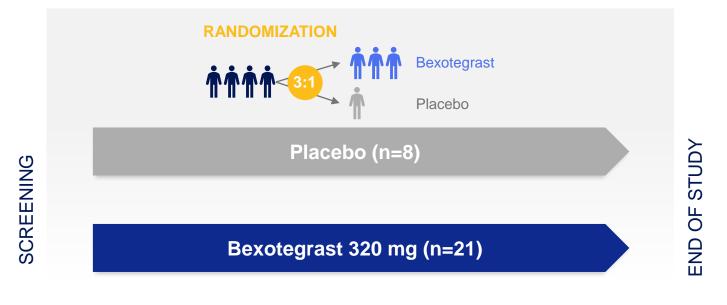
- Evaluate long term safety of the top dose planned for late-stage development
- Evaluate durability of treatment effect (FVC) including symptomatic improvement (cough)
- Assess long-term effects on pulmonary fibrosis as measured through QLF imaging

#### Key Takeaways from the Trial

- Bexotegrast continues to demonstrate a favorable safety and tolerability profile
- Bexotegrast demonstrated durable improvements across physiologic (FVC), radiographic (QLF) and symptomatic (cough) assessments versus placebo
- Data provide strong support to advance bexotegrast into late-stage development



### **INTEGRIS-IPF Study Design and Objectives – Bexotegrast 320 mg Cohort**



#### Stratified for the use of nintedanib or pirfenidone



Treatment duration per protocol: minimum of 24 weeks and a maximum of 48 weeks

PRIMARY AND SECONDARY ENDPOINTS

• Safety, tolerability, PK

#### **EXPLORATORY ENDPOINTS**

- Change in Forced Vital Capacity (FVC) over 12 and 24 weeks
- High Resolution CT-based Quantitative Lung Fibrosis (QLF) imaging
- Patient reported cough severity
- Effect on selected biomarkers



### **Executive Summary – INTEGRIS-IPF 320 mg**

#### **Bexotegrast 320 mg was Well Tolerated Over Long-Term Treatment Up to 40 Weeks**

- Most TEAEs were mild or moderate in severity and not related to study drug
- No discontinuations due to TEAEs from Week 12 to Week 40
- No drug-related SAEs

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#### **Evidence of a Durable Treatment Effect on FVC Over 24 weeks**

- Continued improvement in FVC versus placebo from Week 12 to Week 24
- 50% of bexotegrast-treated patients experienced an increase in FVC from baseline at Week 24 vs. zero on placebo
- Of bexotegrast-treated participants with FVC increase from baseline at Week 12, 89% maintained an increase at Week 24

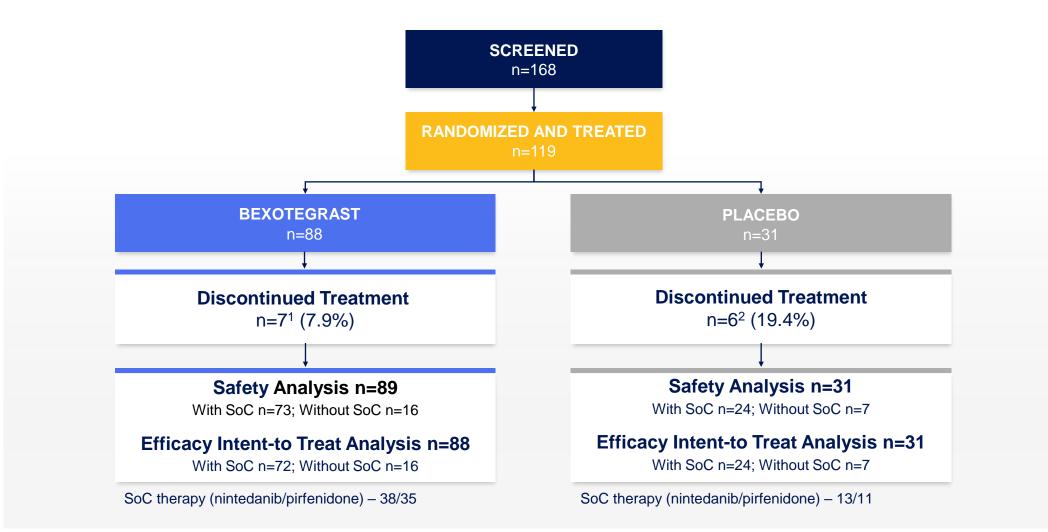
#### Quantitative Lung Fibrosis (QLF) Evaluation Strongly Supports Bexotegrast's Antifibrotic Mechanism

- QLF imaging showed stabilization of fibrosis with bexotegrast while placebo had clinically meaningful progression
- At Week 24, bexotegrast-treated participants were twice as likely to show stabilization or improvement of fibrosis relative to placebo



Bexotegrast reduced patient-reported cough severity in contrast to worsening on placebo

### **INTEGRIS-IPF – Final Participant Disposition**



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### **Baseline Demographics**

Characteristic	Bexotegrast 320mg (n=22)	Placebo (n=8)
Male sex, n (%)	21 (95.5)	5 (62.5)
Female sex, n (%)	1 (4.5)	3 (37.5)
Age (yr), mean (SD)	70.5 (7.14)	73.3 (7.98)
Race, n (%)		
White	21 (95.5)	8 (100)
Other / Not Reported / Unknown	1 (4.5)	0
Weight (kg), mean (SD)	88.5 (15.61)	80.6 (13.18)
Body-mass index (kg/m²), mean (SD)	28.1 (4.08)	27.1 (2.95)

SD = Standard deviation; BMI = Body Mass Index; FVC = Forced Vital Capacity; DLCO = Diffusing capacity for carbon monoxide.



Characteristic	Bexotegrast 320mg (n=22)	Placebo (n=8)
Time since diagnosis of IPF (mo), mean (SD)	34.4 (28.97)	41.6 (32.56)
Standard of Care Use, n (%)	18 (81.8)	6 (75.0)
None	4 (18.2)	2 (25.0)
Nintedanib	10 (45.5)	5 (62.5)
Pirfenidone	8 (36.4)	1 (12.5)
Duration of Standard of Care at Randomization (mo), mean (SD)	23.3 (21.76)	17.8 (20.30)
Baseline FVC (mL)		
Mean (SD)	3,192.0 (678.39)	2,658.4 (587.10)
Median	3,239.0	2,733.3
Percent of predicted value (%), mean (SD)	77.5 (15.83)	75.5 (18.90)
Percent of predicted DLCO, corrected for the hemoglobin level (%), mean (SD)	47.9 (13.18)	49.4 (12.91)
GAP Stage, n (%)		
GAP Stage I	7 (31.8)	3 (37.5)
GAP Stage II	12 (54.5)	5 (62.5)
GAP Stage III	2 (9.1)	0



BMI = Body Mass Index; mo = Month; SD = Standard Deviation; GAP Stage I = GAP Index 0-3; GAP Stage II = GAP Index 4-5; GAP Stage III = GAP Index 6-8. GAP Index score (0-8) derived from Gender, Age, FVC, % Predicted and DLCO, % Predicted.

### **Safety Summary**

AE, n (%) of Participants Reporting	Bexotegrast 320mg (n=22)	Placebo (n=8)
TEAE	20 (90.9)	7 (87.5)
Related to study drug	5 (22.7)	2 (25.0)
Serious TEAE	2 (9.1)	1 (12.5)
Related to study drug	0	0
TEAE of CTCAE Grade 3 or Higher	5 (22.7)	1 (12.5)
Related to study drug	1 (4.5) <sup>1</sup>	0
TEAE Leading to Interruption of Study Drug	4 (18.2) <sup>2</sup>	0
TEAE Leading to Withdrawal of Study Drug	3 (13.6) <sup>2,3,4</sup>	1 (12.5)
TEAE Leading to Early Termination from Study	3 (13.6) <sup>2,3,4</sup>	0
TEAE Leading to Death	1 (4.5) <sup>3</sup>	0

1 - Blood pressure increased; 2 - Abdominal pain/Diarrhea in participant with pre-existing ulcerative colitis;

3 – Acute respiratory failure in a GAP Stage III participant with pre-existing atrial fibrillation 8 days following elective atrioventricular node ablation; 4 – Diarrhea in participant with concomitant use of nintedanib



AE = Adverse Event; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA v. 24.0. TEAE is defined as any AE starting (or worsening) on or after the date of first dose.

### Most Frequently Reported TEAEs Were Not Related to Study Drug

AE, n (%) of Participants Reporting	Bexotegrast 320 mg (n=22)	Placebo (n=8)
Most frequent TEAEs (> 10% in at least one arm)		
Diarrhea	7 (31.8)	3 (37.5)
Related to study drug	4 (18.2) <sup>1</sup>	0
Dyspnoea	5 (22.7)	1 (12.5)
Related to study drug	0	0
Idiopathic Pulmonary Fibrosis	4 (18.2)	0
Related to study drug	0	0
Cough	3 (13.6)	2 (25.0)
Related to study drug	0	0
Upper respiratory tract infection	2 (9.1)	1 (12.5)
Related to study drug	0	0

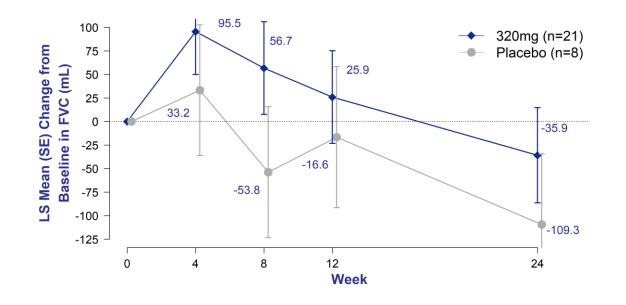
1- Participant with history of sigmoid volvulus, colectomy and colo-colonic anastomosis fell with trauma to his back. Following analgesic treatment with narcotics and NSAIDs, he was hospitalized for sigmoid colon ileus.



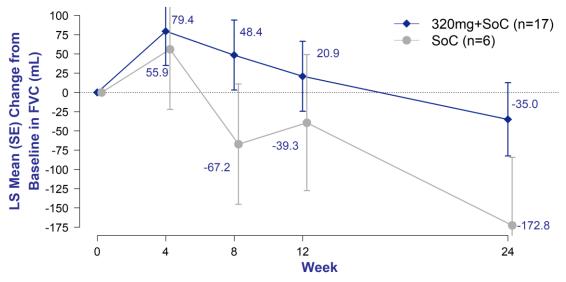
TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA version 24.0. TEAE is defined as any AE starting (or worsening) on or after the date of first dose

## FVC Change from Baseline over 24 Weeks ITT Population vs. SoC Sub-Group

#### **ITT Population**



#### Standard-of-Care Sub-Group



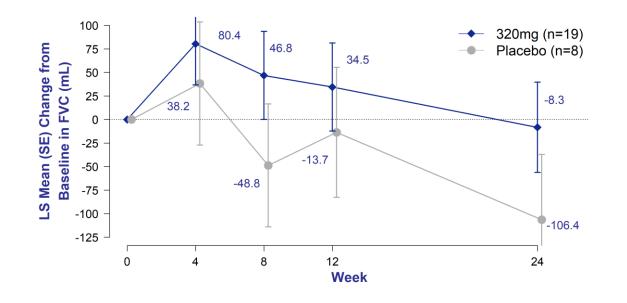
Bexotegrast reduced FVC decline by 67% relative to placebo at Week 24 Bexotegrast + SOC reduced FVC decline by 80% relative to SOC alone at Week 24



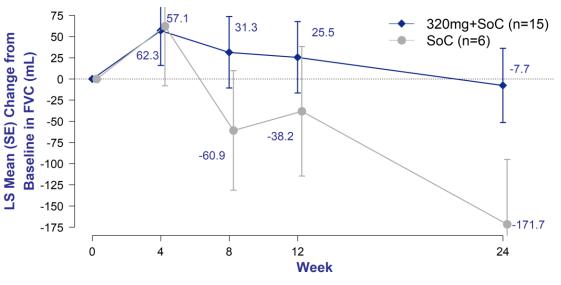
Participants not on SoC not shown due to small sample size, n=4 (320 mg) and n=2 (placebo) FVC = forced vital capacity; ITT=intent to treat; SoC = standard of care (nintedanib or pirfenidone)

## **FVC Change from Baseline over 24 Weeks – Sensitivity Analysis** Trimmed Mean Sensitivity Analysis<sup>1</sup>

#### **ITT Population**



#### Standard-of-Care Sub-Group

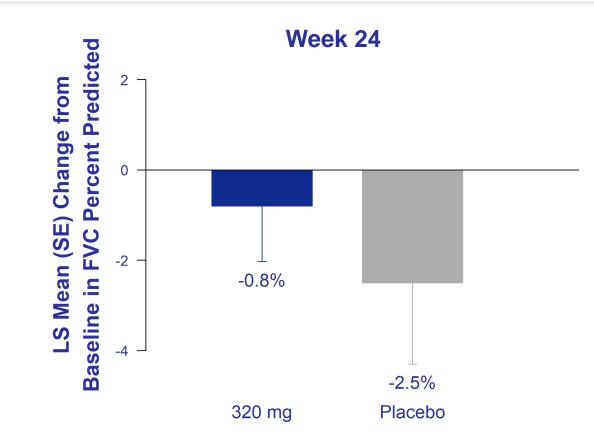


Bexotegrast reduced FVC decline by 92% relative to placebo at Week 24 Bexotegrast + SOC reduced FVC decline by 96% relative to SOC alone at Week 24



1 – Trimmed Mean Sensitivity Analysis excludes the two bexotegrast-treated participants with the highest and lowest FVC values at Week 24 Participants not on SoC not shown due to small sample size, n=4 (320 mg) and n=2 (placebo) FVC = forced vital capacity; ITT=intent to treat; SoC = standard of care (nintedanib or pirfenidone)

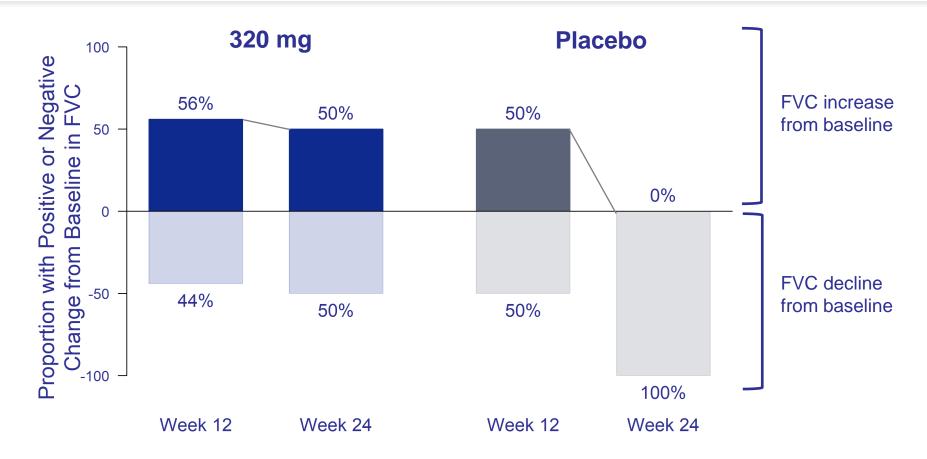
## FVC Percent Predicted Change from Baseline at Week 24 ITT Population



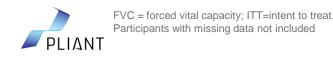
**Bexotegrast reduced the decline in FVCpp by 68% relative to placebo** 



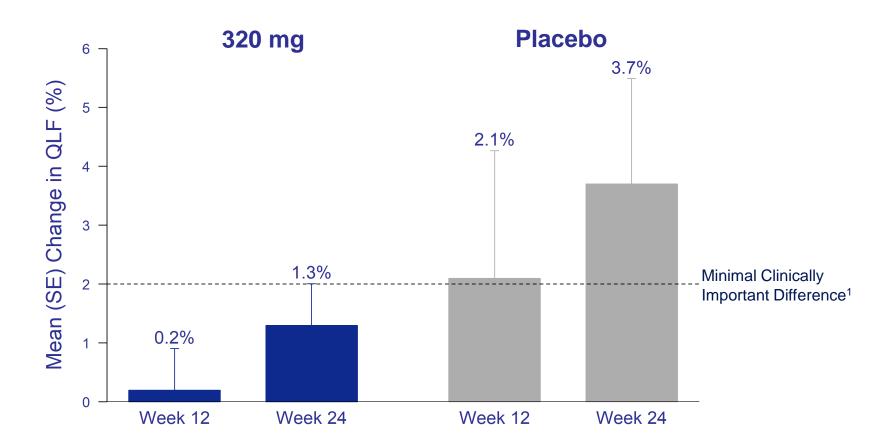
## **Bexotegrast Demonstrated Durable Increase in FVC at Week 24** ITT Population



89% of bexotegrast-treated participants with FVC increase at Week 12 maintained an increase at Week 24



### **QLF Mean Percent Change from Baseline at Weeks 12 and 24** Per CT Protocol Population



Bexotegrast group demonstrated stabilization of fibrosis, in contrast to placebo group which showed clinically meaningful progression at Weeks 12 and 24

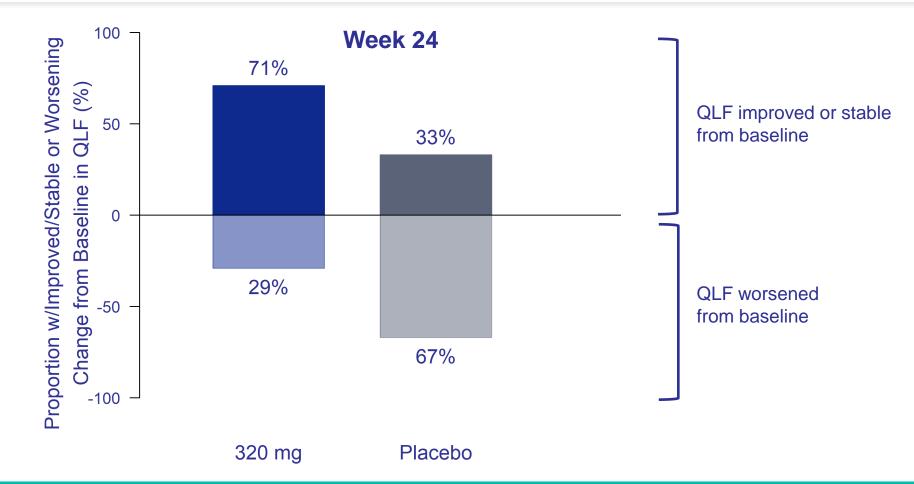


QLF = quantitative lung fibrosis; QLF Minimal Clinically Important Difference for whole lung: 2%; stable disease (-2%, 2%) Per CT protocol population: Participants with both baseline and post baseline high resolution computed tomography (HRCT) scans meeting evaluability criteria per Imaging Charter 1 - *EU Radiology* 2020 30:726-734

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### More Patients on Bexotegrast Showed Stabilization of Fibrosis at Week 24 Per CT Protocol Population

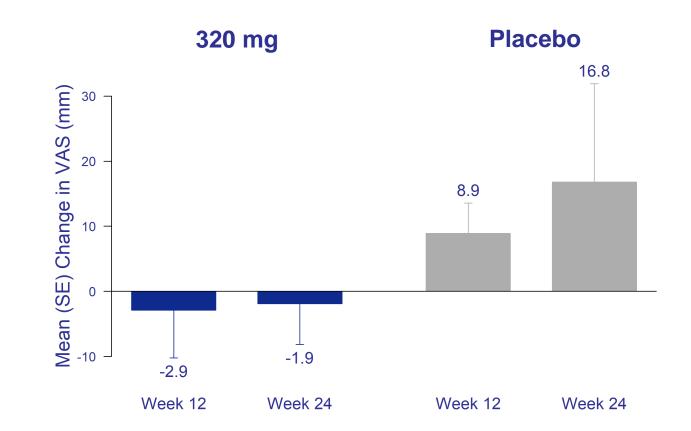


At Week 24, bexotegrast-treated participants were more than twice as likely to show stabilization or improvement of fibrosis relative to placebo



QLF = quantitative lung fibrosis; QLF Minimal Clinically Important Difference for whole lung: 2%; Improved disease <-2%, Stable disease (-2%, 2%), Worsened disease >2% Per CT protocol population: Participants with both baseline and post baseline high resolution computed tomography (HRCT) scans meeting evaluability criteria per Imaging Charter

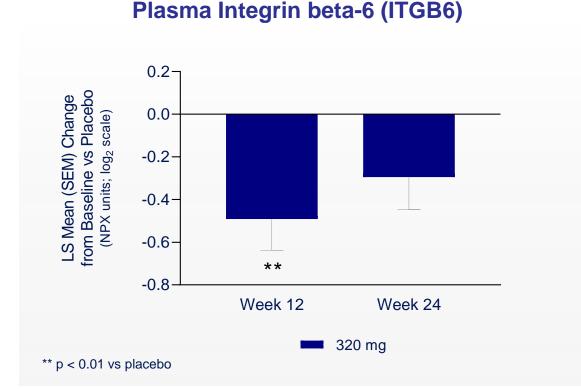
## Cough Severity Visual Analog Scale (VAS) Change from Baseline ITT Population



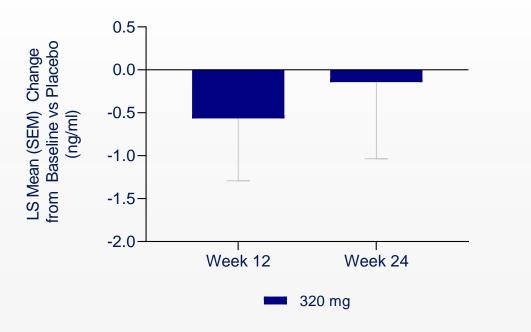
Chronic cough in IPF is an independent predictor of disease progression and mortality<sup>1</sup>



### Bexotegrast Reduced Circulating Biomarkers ITGB6 and PRO-C3 Relative to Placebo



Serum PRO-C3 Type III collagen synthesis neoepitope



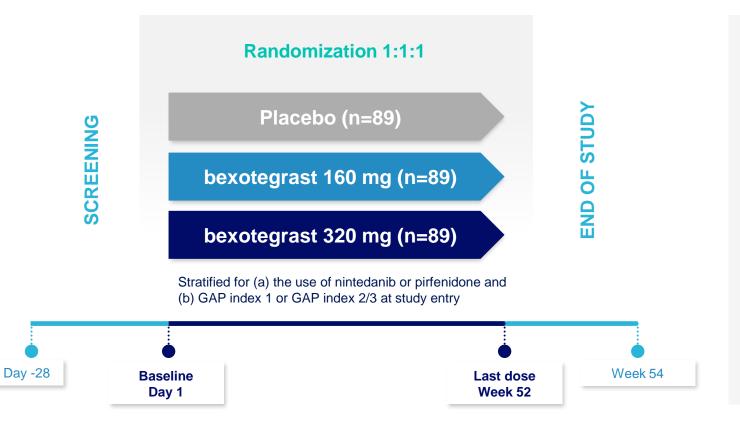
## Elevated integrin beta-6 plasma levels shown to be associated with ILD progression over 12 months<sup>1</sup>

PRO-C3 shown to be elevated in patients with IPF and associated with progressive disease<sup>2</sup>



1- Lancet Respir Med. 2022 Jun;10(6):593-602; 2 - Respir Res. 2019 Jul 12;20(1):148.
LS = Least Squares; SE = Standard Error; Integrin beta-6 data reported in relative quantitation log<sub>2</sub> scale

#### **BEACON-IPF** Phase 2b Study Design



#### **PRIMARY ENDPOINT**

 Change from baseline in absolute FVC (mL) at Week 52

#### SECONDARY ENDPOINTS

- Time to disease progression (≥10% absolute decline from baseline in (FVCpp), respiratory-related hospitalization, or all-cause mortality)
- Change from baseline in absolute FVC (mL) in participants on and off background therapy
- Change from baseline in Living with Pulmonary Fibrosis total score at Week 52
- Safety and Tolerability



## Toby Maher, M.D., Ph.D.,

Professor of Medicine and Director of Interstitial Lung Disease at Keck School of Medicine, University of Southern California, Los Angeles



# Bernard Coulie, M.D., Ph.D. President and Chief Executive Officer



# **Question and Answer Session**



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