

The logo for ERS Congress 2024, featuring a red circle with a white grid pattern inside, followed by the text "ERS CONGRESS | 2024" in white.

# ERS CONGRESS | 2024

7-11 September | Vienna, Austria

## Safety and tolerability of bexotegrast in Phase 2 trials of idiopathic pulmonary fibrosis (IPF) and primary sclerosing cholangitis (PSC)

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I have no real or perceived conflicts of interest that relate to this presentation.

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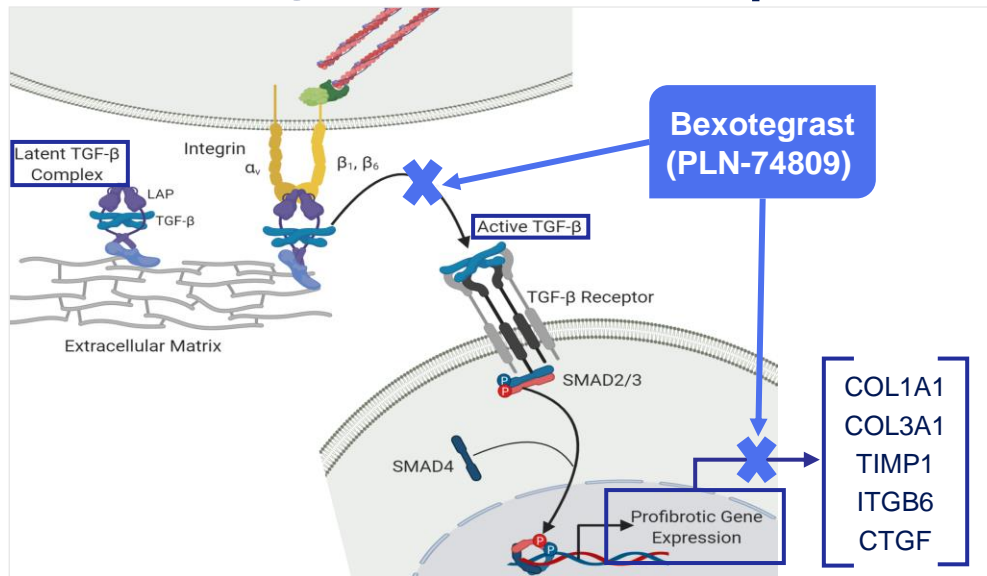
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<b>Other support / potential conflict of interest:</b>	Employee of Pliant Therapeutics, Inc. This study was sponsored by Pliant Therapeutics, Inc. Editorial assistance was provided by Samantha O'Dwyer, PhD, of Nucleus Global and funded by Pliant Therapeutics, Inc. This presentation was developed in accordance with Good Publication Practice (GPP 2022) guidelines. Bexotegrast is an investigational drug in which safety and efficacy are still being evaluated and is not approved by any health authority.
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## $\alpha_v\beta_6$ and $\alpha_v\beta_1$ Integrins Promote Fibrosis Through Activation of TGF- $\beta$ <sup>1,2,a</sup>



- TGF- $\beta$  is a central driver of fibrosis<sup>1,2</sup>
- Systemic TGF- $\beta$  blockade carries toxicity risks<sup>2</sup>
- Activation of latent TGF- $\beta$  by  $\alpha_v\beta_6$  (lung epithelial cells, injured cholangiocytes) and  $\alpha_v\beta_1$  (lung fibroblasts, HSCs) is increased in fibrotic tissue<sup>2-8</sup>

**Localized TGF- $\beta$  inhibition in fibrotic tissue, by targeting  $\alpha_v\beta_6$  and  $\alpha_v\beta_1$  with bexotegast, may provide a novel approach to treat IPF and PSC without potentially affecting TGF- $\beta$  signaling systemically**

## Objective:

To provide a comprehensive safety analysis of bexotegast across Phase 2 clinical studies of 12 weeks or longer in IPF and PSC

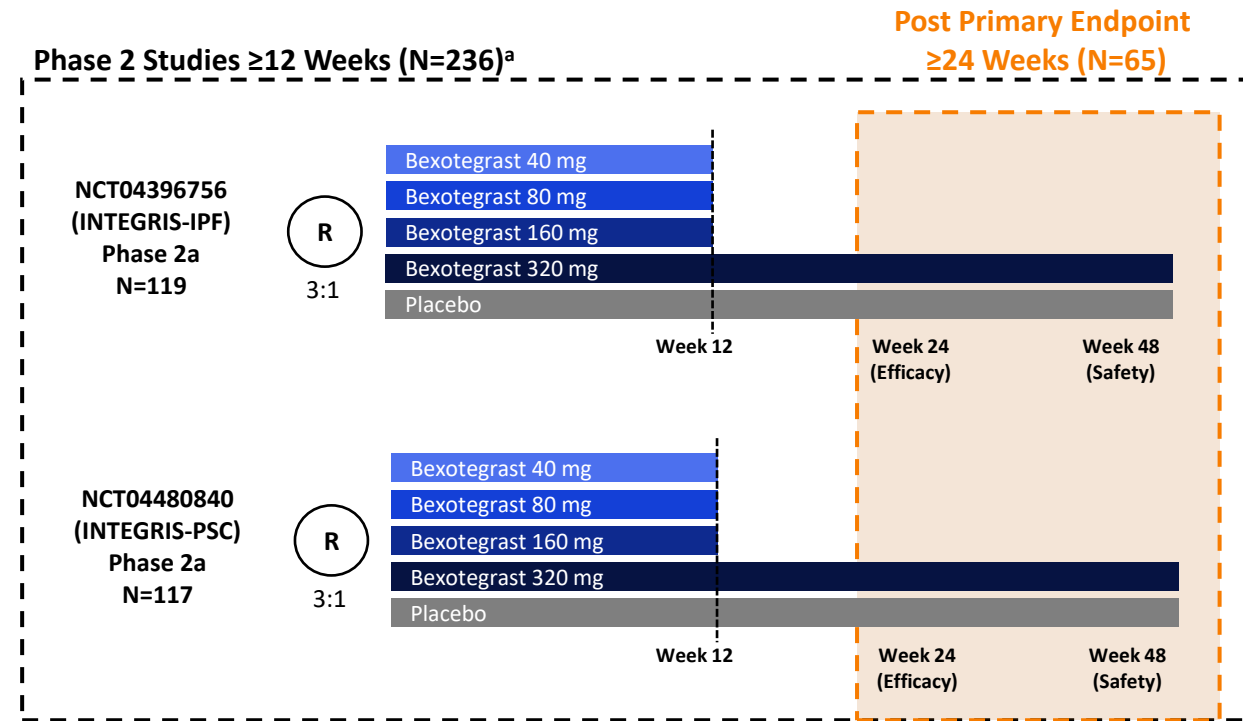
1. Saito A, et al. *Int J Mol Sci*. 2018;19(8):2460; 2. Decaris ML, et al. *Respir Res*. 2021;22(1):265; 3. Reed NI, et al. *Sci Transl Med*. 2015;7(288):288ra79; 4. Munger JS, et al. *Cell*. 1999;96(3):319-328; 5. Horan GS, et al. *Am J Respir Crit Care Med*. 2008;177(1):56-65; 6. Saini G, et al. *Eur Respir J*. 2015;46(2):486-494; 7. Peng Z-W, et al. *Hepatology*. 2016;63(1):217-23; 8. Schaub J, et al. *J Hepatol*. 2019;70(1):E57-E58.

<sup>a</sup> This image is based off of preclinical animal models.

COL1A1, collagen type I alpha 1; COL3A1, collagen type III alpha 1; CTGF, connective tissue growth factor; HSC, hepatic stellate cell; IPF, idiopathic pulmonary fibrosis; ITGB6, integrin beta-6; LAP, latency-associated peptide; PSC, primary sclerosing cholangitis; SMAD, family of proteins similar to the gene products of the *Drosophila* gene 'mothers against decapentaplegic homolog 1' (MAD) and the *C. elegans* gene SMA; TGF- $\beta$ , transforming growth factor-beta; TIMP1, tissue inhibitor matrix metalloproteinase 1.

# Studies Included in the Safety Population

- To date, over 700 participants have been exposed to bexotegrast in unblinded and blinded studies
- This safety analysis was performed on completed Phase 2 studies of  $\geq 12$  weeks treatment duration
- Bexotegrast doses ranged from 40 to 320 mg once daily

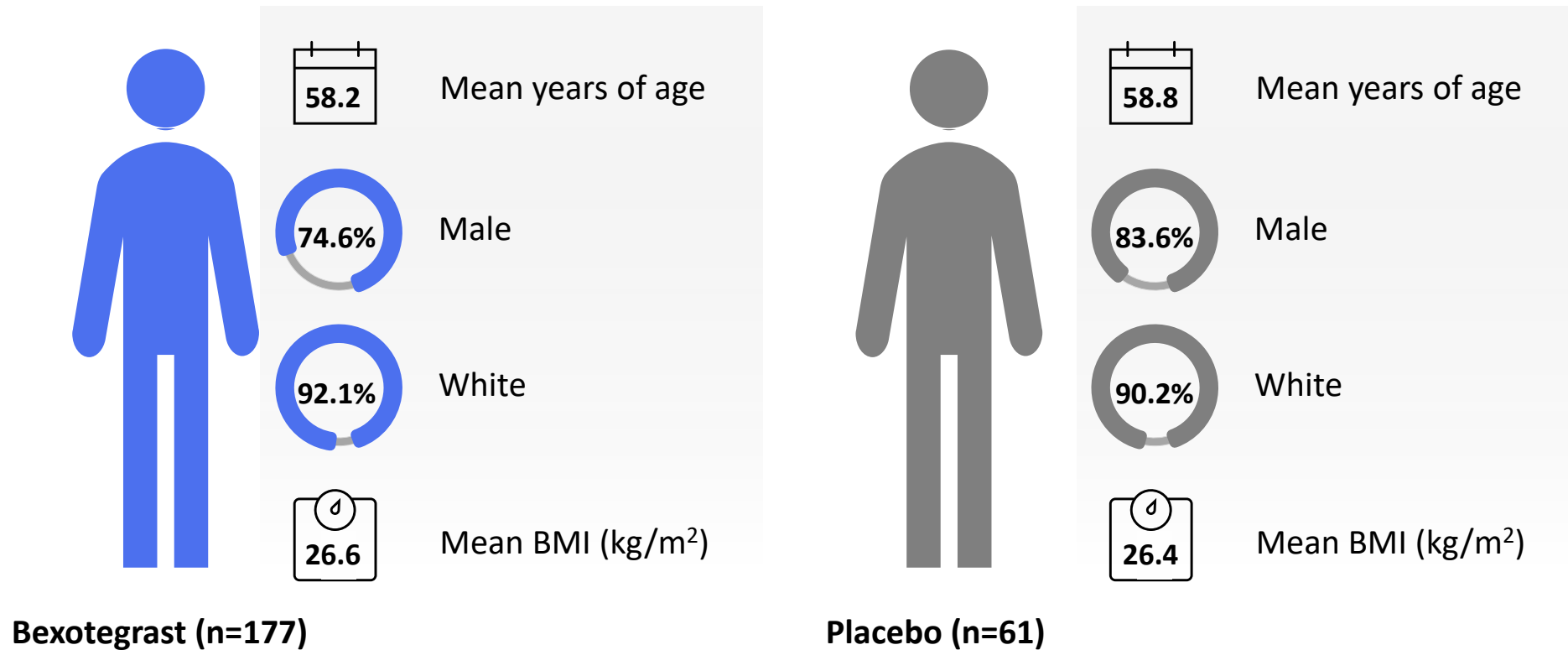


Number of participants (%)	Bexotegrast <sup>a</sup> (n=177)	Placebo <sup>a</sup> (n=61)
Safety $\leq 12$ weeks	177 (98.3)	61 (100)
Safety data $> 12$ weeks	167 (92.8)	58 (95.1)
Post primary endpoint $\geq 24$ weeks	49 (27.7)	17 (27.9)

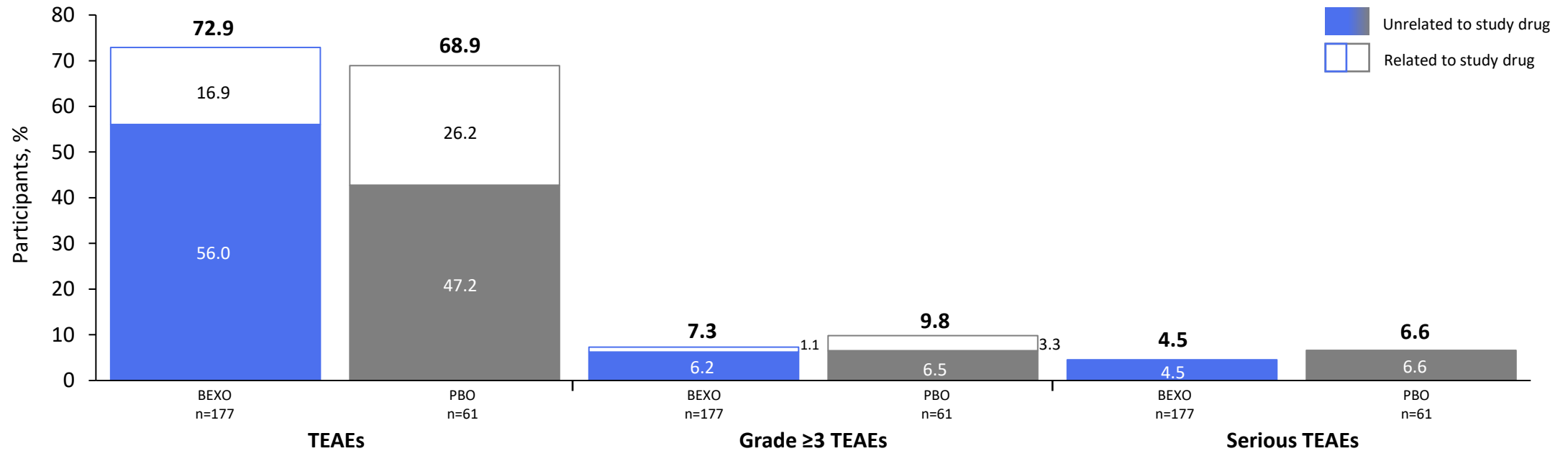
<sup>a</sup> Four participants in INTEGRIS-PSC participated in 2 cohorts; 3 participants received bexotegrast in both cohorts and are counted once in the all bexotegrast column; 1 participant received bexotegrast in one cohort and received placebo in the other cohort and is counted in both the bexotegrast column and in the placebo column. Each of the participants who repeated a cohort is counted once in the total column. One participant in INTEGRIS-IPF received both placebo and bexotegrast due to incorrect study drug dispensation and is counted in both treatment groups. The participant is counted once in the total column.  
IPF, idiopathic pulmonary fibrosis; PSC, primary sclerosing cholangitis; R, randomization.

# Baseline Demographics

## Phase 2 Studies $\geq 12$ Weeks Treatment Duration (N=236)



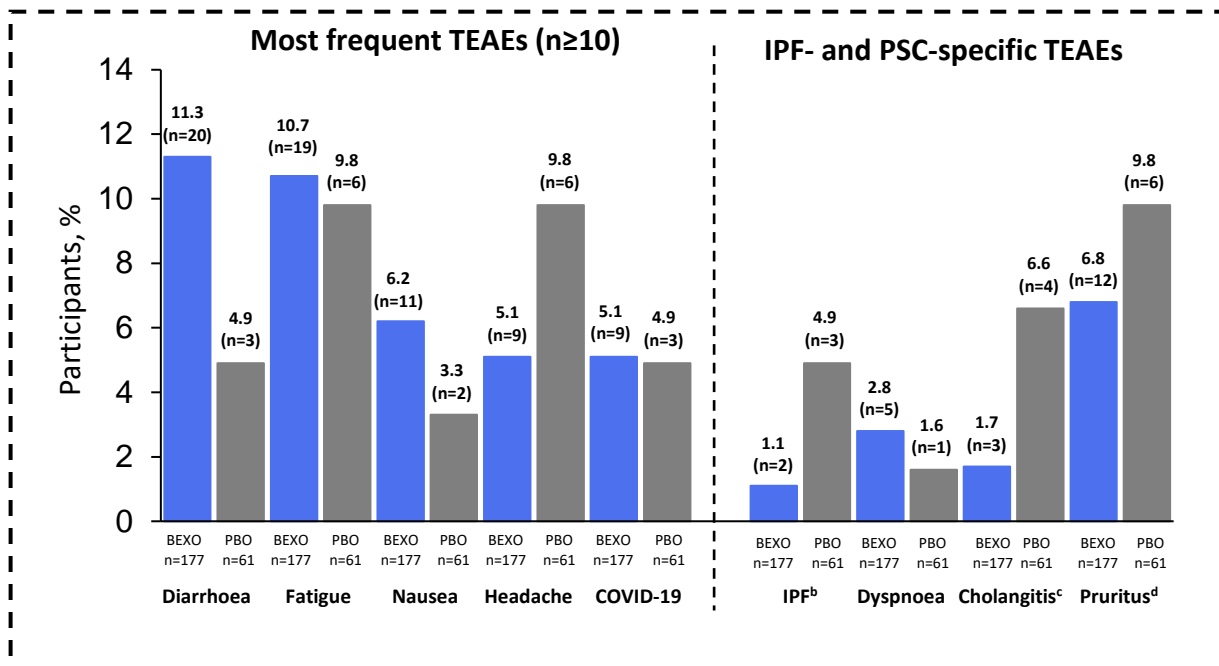
## Phase 2 Studies ≥12 Weeks Treatment Duration (N=236)



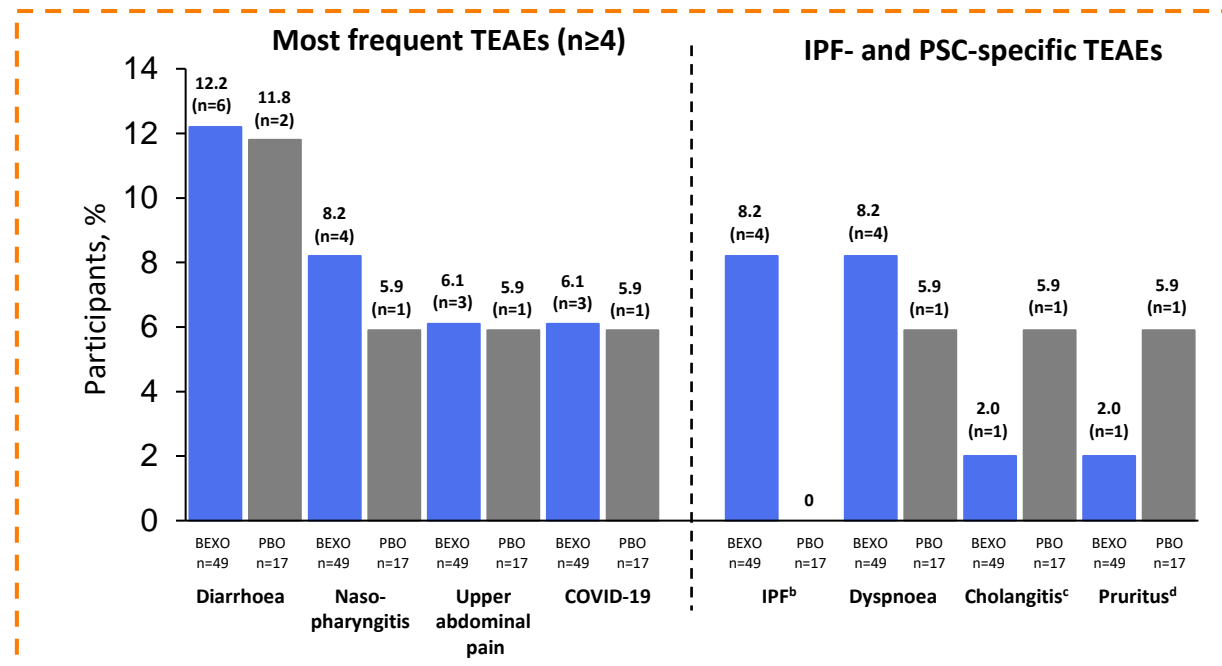
- Rates of discontinuation were similar between bexotegrast- and placebo-treated participants (2.3% vs 3.3%, respectively)
- Grade ≥3 TEAEs and serious TEAE rates were higher in the placebo group compared with the bexotegrast group
- No SAEs were considered related to the study drug

# Most Frequently Reported TEAEs

## TEAEs In Participants with Treatment Duration ≤12 Weeks



## TEAEs In Participants with Treatment Duration >12 Weeks<sup>a</sup>



- ▶ The proportion of bexotegrast-treated participants reporting TEAEs was similar regardless of time receiving study drug
- ▶ No more than 12% of participants reported any one TEAE across treatment durations

<sup>a</sup> Treatment duration of >12 weeks and up to 40 weeks.

<sup>b</sup> Includes IPF and pulmonary fibrosis.

<sup>c</sup> Includes cholangitis and sclerosing cholangitis.

<sup>d</sup> Includes pruritis and cholestatic pruritis.

BEXO, bexotegrast; IPF, idiopathic pulmonary fibrosis; PBO, placebo; PSC, primary sclerosing cholangitis; TEAE, treatment-emergent adverse event.

## **Bexotegrast was well tolerated in participants in 2 Phase 2 studies $\geq 12$ weeks in duration**

- The safety profile of bexotegrast was similar for participants treated for  $\geq 12$  weeks compared to those treated for a shorter duration

## **The most frequently reported TEAE in bexotegrast-treated participants was diarrhea**

- The most common TEAE  $\leq 12$  weeks was diarrhoea (11.3%)
- The most common TEAEs  $> 12$  weeks was diarrhoea (12.2%)

## **Most TEAEs were mild or moderate**

- Discontinuation rates were low in bexotegrast-treated participants (2.3%)

## **Late-stage evaluation of bexotegrast in participants with IPF is currently underway (BEACON-IPF; NCT06097260)**





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- 3 Reed NI, et al. *Sci Transl Med*. 2015;7(288):288ra79.
- 4 Munger JS, et al. *Cell*. 1999;96(3):319-328.
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