Phase 2a Collagen PET Study of Bexotegrast Topline Results
Quantification of Collagen in the Lung using PET Imaging

- $^{68}$Ga-CBP8 is a PET probe that binds type I collagen with high specificity\(^1\)
- IPF patients have higher standardized uptake values (SUV) compared to healthy volunteers\(^2\)
- The probe binds to both freshly synthesized and mature collagen
- $^{68}$Ga-CBP8 previously detected treatment response to anti-fibrotic therapy in a mouse model of pulmonary fibrosis\(^1\)

Note: Uptake in the heart and vasculature as well as in the liver is to be expected based on the probe’s half-life and biodistribution.

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68GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope
SUV: standardized uptake value; SUV measures the ratio of the uptake of a radiotracer in tissue
\(^1\)Désogere et al, Sci Trans Med. 2017; \(^2\)Montesi Am J Respir Crit Care Med 200:2 2019
Design and Objectives
Quantification of Type 1 Collagen in the Lung using PET Imaging

PRIMARY AND SECONDARY ENDPOINTS
• Change in whole lung standardized uptake value (SUV) of $^{68}$Ga-CBP8 (type-1 collagen probe)
• Safety and tolerability

EXPLORATORY ENDPOINTS
• Changes in FVC and FVCpp
• Change in VAS for cough severity
• Changes in fibrosis biomarkers

INCLUSION CRITERIA
• Diagnosis of IPF (within 8 years)
• FVC percent predicted $\geq 45$
• DLCO $\geq 30$
• Estimated glomerular filtration rate $\geq 50$mL/min

RANDOMIZATION
2:1
Bexotegrast
Placebo

SCREENING
Placebo (n=3)
Bexotegrast 160 mg (n=7)

Placebo (n=3)

Stratified for the use of SoC (nintedanib or pirfenidone)

Day -28
Baseline
Day 1
Last dose
Week 12
Week 14

FVC: forced vital capacity, FVCpp: forced vital capacity percent predicted; SoC = Standard of care; VAS: visual analog scale
$^{68}$GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope
Participant Disposition

SCREENED
n=14

RANDOMIZED AND TREATED
n=10

BEXOTEGRAST

Safety Population$^3$ n=7
With SoC n=6 (86%)
Efficacy Intent-to Treat Analysis n=7

Discontinued Treatment
n=0

PLACEBO

Safety Population$^3$ n=3
With SoC=2 (67%)
Efficacy Intent-to Treat Analysis n=3

Discontinued Treatment
n=0

SoC = Standard of care
## Baseline Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bexotegrast 160mg (n=7)</th>
<th>Placebo (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male sex, n (%)</strong></td>
<td>6 (85.7)</td>
<td>3 (100)</td>
</tr>
<tr>
<td><strong>Age (yr), median (IQR)</strong></td>
<td>70 (64 – 72)</td>
<td>74 (72 – 76)</td>
</tr>
<tr>
<td><strong>Weight (kg), median (IQR)</strong></td>
<td>81.2 (79.0 – 88.5)</td>
<td>78.0 (77.6 – 85.3)</td>
</tr>
<tr>
<td><strong>BMI (kg/m²), median (IQR)</strong></td>
<td>25.7 (23.7 – 30.4)</td>
<td>26.4 (24.0 – 30.3)</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>6 (85.7)</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Black</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (14.3)</td>
<td>0</td>
</tr>
<tr>
<td>Other / Not Reported / Unknown</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

IQR = Interquartile range (Q1, Q3); BMI = Body Mass Index
## Baseline Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bexotegrast 160mg (n=7)</th>
<th>Placebo (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time since diagnosis of IPF (mo), median (IQR)</strong></td>
<td>50 (22 – 70)</td>
<td>9 (7 – 72)</td>
</tr>
<tr>
<td><strong>Standard of Care Use, n (%)</strong></td>
<td></td>
<td></td>
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<tr>
<td>Nintedanib</td>
<td>5 (71.4)</td>
<td>1 (33.3)</td>
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<tr>
<td>Pirfenidone</td>
<td>1 (14.3)</td>
<td>1 (33.3)</td>
</tr>
<tr>
<td><strong>Duration of Standard of Care at Randomization (mo), median (IQR)</strong></td>
<td>34.5 (17 – 55)</td>
<td>40.0 (6 – 74)</td>
</tr>
<tr>
<td><strong>FVC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute (mL), median (IQR)</td>
<td>2,750 (2,400 – 3,080)</td>
<td>2,250 (1,700 – 2,640)</td>
</tr>
<tr>
<td>Percent of predicted value (%), median (IQR)</td>
<td>66.0 (56.0 - 92.0)</td>
<td>58.0 (49.0 - 69.0)</td>
</tr>
<tr>
<td><strong>Percent of predicted DLCO, corrected for the hemoglobin level (%), median (IQR)</strong></td>
<td>49 (40.0 – 58.0)</td>
<td>43 (36.5 – 45.0)</td>
</tr>
<tr>
<td><strong>GAP Stage, n (%)</strong></td>
<td></td>
<td></td>
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<tr>
<td>GAP Stage I</td>
<td>4 (57.1)</td>
<td>0</td>
</tr>
<tr>
<td>GAP Stage II</td>
<td>2 (28.6)</td>
<td>2 (66.7)</td>
</tr>
<tr>
<td>GAP Stage III</td>
<td>1 (14.3)</td>
<td>1 (33.3)</td>
</tr>
</tbody>
</table>

GAP Index score derived from Gender, Age, FVC, % Predicted and DLCO, % Predicted.
IQR = Interquartile range (Q1, Q3); DLCO= Diffusing Capacity for Carbon Monoxide; FVC = Forced Vital Capacity
Key Findings

**Bexotegrast cohort showed reduced PET ligand standardized uptake values (SUV) compared to placebo**
- Reduction in SUV post-treatment indicates less total lung collagen, suggesting potential reversal of fibrosis
- Additional support of bexotegrast’s antifibrotic mechanism of action

**No new safety concerns identified over 12 weeks of treatment**
- Most adverse events were mild with no study discontinuations observed
- No SAEs observed

**Bexotegrast cohort showed improved lung function and decreased cough severity across all timepoints**
- Positive FVC change compared to decline in placebo across all time points
- Decrease in cough severity observed at all time points compared to worsening seen on placebo

**Biomarker results further support bexotegrast’s antifibrotic mechanism**
- Bexotegrast cohort showed reduced circulating PRO-C3 and Integrin Beta-6 levels at Weeks 4 and 12 compared to placebo
Safety Overview

- No serious adverse events (SAEs) occurred in the trial
- Most treatment emergent adverse events (TEAEs) were mild in nature
- No study discontinuations occurred
- Bexotegrast continues to demonstrate a favorable safety and tolerability profile in the IPF patient population
Bexotegrast Showed Reduced PET Tracer SUV Compared to Placebo

ITT Population

Reduction in post-treatment SUV indicates a reduction in total lung collagen

Reduced post-treatment total lung collagen suggests potential reversal of fibrosis

*SUV = Standardized Uptake Value; SE = Standard Error; ^68Ga-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope
SUV measures the ratio of the uptake of a radiotracer in tissue; Top quartile SUV is the mean of SUVs within the top quartile for each lung section; Whole lung is the average of the left and right lungs

Montessi AJRCCM 200:2 2019
Clearly Visible Reduction of Total Lung Collagen

**PARTICIPANT A**
- Bexotegrast 160 mg for 12 weeks
- Decrease in SUV_Q4, -0.17 (-15.5%)
- Improvement in FVC, 130 mL

**PARTICIPANT B**
- Placebo for 12 weeks
- Increase in SUV_Q4, 0.21 (18.4%)
- Decline in FVC, -180 mL

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SUV = Standardized Uptake Value; SUV_Q4: top quartile SUV; 68GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope
FVC: forced vital capacity; VAS: visual assessment scale for cough severity (0-100)
SUV measures the ratio of the uptake of a radiotracer in tissue and quantifies the amount of type I collagen detected.
Bexotegrast Showed Improved Lung Function Compared to Placebo
ITT Population

Bexotegrast cohort maintained a clear separation from placebo at all time points

Note: One placebo subject did not have FVC that meet quality standards per ATS guidelines at Weeks 4, 8 and 12
LS = Least Squares; SE = Standard Error; FVC = Forced Vital Capacity; FVCpp = Forced Vital Capacity Percent Predicted
Bexotegrast showed decreased cough severity compared to placebo ITT population.

**Cough Severity Over 12 Weeks of Treatment**

Graph showing mean (SE) change from baseline in VAS score over 12 weeks of treatment.

- **Bexotegrast cohort** experienced decreased cough severity across all timepoints compared to increased severity on placebo.

EOT: end of treatment; SE: standard error; VAS = Visual Analog Scale
Cough VAS measures patient reported cough severity over last 2 weeks on scale of 0-100 mm.
Bexotegrast Showed Reduced Fibrosis Biomarkers Compared to Placebo

ITT Population

PRO-C3 has been shown to be elevated in patients with IPF and associated with progressive disease.\(^3\)

Elevated ITGB6 plasma levels have been shown to be associated with ILD progression.\(^4\)


ITGB6: Integrin Beta 6; LS = Least Squares; PRO-C3 = Type III Collagen Synthesis Neoepitope; SE = Standard Error
Bexotegrast – Demonstrated Antifibrotic activity

- Bexotegrast continues to demonstrate antifibrotic activity as assessed using a novel PET tracer which measures total lung collagen, and with established serum biomarkers of fibrosis and ILD progression.

- PET results build upon previous evidence of Bexotegrast’s antifibrotic mechanism of action using quantitative lung imaging.

- Bexotegrast cohort showed improvements in lung function and decreases in cough severity across all time points compared to placebo.

- Bexotegrast continues to demonstrate a favorable safety and tolerability profile in the IPF patient population.

- Bexotegrast 160 and 320 mg are currently being evaluated in a global Phase 2b/3 study.