ASSESSMENT OF THE EFFECTS OF GLPG1690 IN IDIOPATHIC PULMONARY DISEASE (IPF) PATIENTS USING FUNCTIONAL RESPIRATORY IMAGING (FRI)

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FRI: A BIOMARKER TO ASSESS TREATMENT EFFICACY

FUNCTIONAL RESPIRATORY IMAGING

- Development of proprietary Functional Respiratory Imaging (FRI), a combination of
  - High Resolution CT Thorax (HRCT)
  - Flow simulations (Computational Fluid Dynamics, CFD)

- FRI provides regional information about
  - Lung structure (HRCT measurements)
  - Lung function (flow simulation)

- FRI is a sensitive biomarker that reduces
  - Study sample size
  - Study time
  - Overall Drug Development Cost
FRI IN IPF POPULATION
A study with HRCT scans of 4 IPF patients compared with matched healthy volunteers showed that IPF patients have:

- More Fibrosis
- Smaller Lung Lobes
- Larger Airways

Vos, Wim, et al. ATS 2015
A study with HRCT scans of 12 IPF patients showed that the disease is more pronounced in the lower lobes:

De Backer, Jan, et al. ATS 2015
FRI IN IPF POPULATION

IPF DISEASE PROGRESSION

• Single arm study with 66 IPF patients with HRCT scans at Baseline, Week 24 and Week 48

• The specific airway radius increases with progressing disease

• Lobar volumes decrease with progressing disease

• The lower lobes are more affected than the upper lobes

Mignot, B., et al. ERS 2017
FRI IN IPF POPULATION

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Mignot, B., et al. ERS 2017
GLPG1690 PHASE IIa TRIAL
GALAPAGOS GLPG1690 PHASE IIa

Study Design

- Exploratory, randomized, double-blind, placebo-controlled trial
- GLPG1690: novel selective autotaxin inhibitor (Galapagos, Belgium)

GLPG1690, oral, 600 mg once daily (n=17) or Placebo (n=6)

Baseline Spirometry HRCT

W1, W2, W4, W8 Spirometry

Week 12 Spirometry HRCT

| Primary Objectives | - Safety & tolerability  
| - PK & PD properties |

| Secondary Objectives | - Pulmonary function by spirometry  
| Functional respiratory imaging (FRI) parameters  
| - Biomarkers  
| - Quality of life measurements |

| Treatment Duration | 12 Weeks treatment and 2 weeks follow-up |

| Patients with HRCT scans at both Baseline and Week 12 | - GLPG1690: 15  
| - Placebo: 3 |
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Baseline Spirometry HRCT

W1, W2, W4, W8 Spirometry HRCT

Week 12 Spirometry HRCT

FVC (L), change from baseline (Mean ±SE)

<table>
<thead>
<tr>
<th>Week</th>
<th>N</th>
<th>FVC (L)</th>
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<tbody>
<tr>
<td>BSL</td>
<td>6</td>
<td>-0.03</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>+0.04</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td>+0.01</td>
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<tr>
<td>12</td>
<td>4</td>
<td>-0.02</td>
</tr>
<tr>
<td>FU</td>
<td>4</td>
<td>-0.02</td>
</tr>
</tbody>
</table>

* p < 0.05

FVC = Forced vital capacity  BSL = baseline  FU = follow up
FRI RESULTS

GALAPAGOS GLPG1690 PHASE IIa

SPECIFIC AIRWAY VOLUME
TOTAL LUNG CAPACITY

**LUNG, TOTAL**
Active vs Placebo Change from baseline: p = 0.0181

Change in Specific Airway Volume [mL/L] at TLC

GLPG1690: N = 15
(0.079±1.917)

PLACEBO: N = 3
(3.038±2.375)
FRI RESULTS

GALAPAGOS GLPG1690 PHASE IIa

SPECIFIC AIRWAY RESISTANCE
TOTAL LUNG CAPACITY

LUNG, TOTAL
Active vs Placebo Change from baseline: p = 0.0334
FRI RESULTS

GALAPAGOS GLPG1690 PHASE IIa

PERCENT PREDICTED LOBAR VOLUMES

TOTAL LUNG CAPACITY

LUNG, TOTAL
Active vs Placebo Change from baseline: p = 0.5153

Change in Lung Volume [%pred] at TLC

GLPG1690: N = 15
(-6.77±15.602)

PLACEBO: N = 3
(-0.70±6.145)
RESPONSE IMAGES OF A REPRESENTATIVE ACTIVE PATIENT

GALAPAGOS GLPG1690 PHASE IIa

RESPONSE IMAGES
ACTIVE PATIENT

TLC Specific Airway Volume change
FRC Lobe Volume change
TLC Lobe Volume change
RESPONSE IMAGES OF A REPRESENTATIVE PLACEBO PATIENT

GALAPAGOS GLPG1690 PHASE IIa

RESPONSE IMAGES
PLACEBO PATIENT

TLC Specific Airway Volume change

FRC Lobe Volume change

TLC Lobe Volume change
CONCLUSIONS

• Results of this exploratory study provided preliminary efficacy signals:
  • FRI shows a benefit of GLPG1690 over placebo for airway parameters
  • Lobar parameters show no differences between both groups
  • FVC remained around baseline levels for active patients after 12 weeks

• Limitations:
  • Study was not designed to investigate efficacy
  • Small patient numbers with available serial scans, particularly in the placebo group (n=3)

• It is worthwhile to further assess relevant FRI parameters in subsequent (placebo-controlled) trials in IPF population as encouraged in a letter of support from the FDA