FGCL-3019-079 OVERVIEW
Open-Label, Single-Arm Phase 2 Study in Non-Ambulatory Subjects with Duchenne Muscular Dystrophy

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PROJECT PARENT MUSCULAR DYSTROPHY 2018
ANNUAL CONFERENCE
Pamrevlumab Background

Pamrevlumab (FG-3019): a novel investigational agent for treating fibrotic and fibro-proliferative diseases

- Pamrevlumab is a recombinant human monoclonal antibody that inhibits the activity of connective tissue growth factor (CTGF), a critical mediator in the progression of fibrosis and related serious diseases. Pamrevlumab has been studied in several indications including pancreatic ductal adenocarcinoma (PDAC) and idiopathic pulmonary fibrosis (IPF).
- 11 Phase 1 and Phase 2 clinical trials completed or ongoing
- Approximately 530 patients have received pamrevlumab
- About half of the patients have received treatment for >6 months

Pancreatic cancer

- Completed Phase 1/2 trial in 75 patients showing dose-related improvement in survival (J Cancer Clin Trials 2017, 2:1)
- Ongoing Phase 1/2 trial in 37 patients with locally advanced unresectable pancreatic cancer
- All patients completed treatment and are currently in long-term follow-up
Pamrevlumab Background

Idiopathic Pulmonary Fibrosis (IPF)

- Completed a one-year, open-label Phase 2 trial in 89 patients showing reversal of lung fibrosis and improved lung function in some patients (*Eur Respir J* 2016; 47: 1481–1491)
- Completed randomized, placebo-controlled Phase 2b trial with 103 patients (PRAISE study)
- Pamrevlumab did better than placebo at preserving lung function according to FVC measurements
- Study results presented at the ERS International Congress 2017 and the ATS International Conference in 2018

Safety

- No safety signals to date that might prevent further development of the drug
- Well tolerated and no dose-limiting toxicities observed to date
PRAISE in IPF

Randomized, Double-Blind, Placebo-Controlled Phase 2 Study to Evaluate the Safety and Efficacy of Pamrevlumab (FG-3019) in Patients with Idiopathic Pulmonary Fibrosis
Efficacy Analysis from PRAISE, Primary Endpoint*: Mean Change from Baseline at Week 48 in FVC Random Coefficients Model (Linear Slope Method)

**FVC%-Predicted**

- **Pamrevlumab**
  - Mean FVC% change: 
  - Mean FVC% change: -2.85 
  - +/-0.79
  - Mean FVC% change: -7.17 
  - +/-1.86

- **Placebo**
  - Mean FVC% change: 
  - Mean FVC% change: -5.72 
  - +/-1.1

**p-value** = 0.0331

**FVC%-Predicted Difference**: 4.33%

**Relative Difference**: 60%

**FVC (mL)**

- **Pamrevlumab**
  - Mean FVC change (mL): 
  - Mean FVC change (mL): -129 
  - +/-27.1

- **Placebo**
  - Mean FVC change (mL): 
  - Mean FVC change (mL): -308 
  - +/-74.3

**p-value** = 0.0249

**Absolute FVC Difference**: 178mL

**Relative Difference**: 58%
Safety Summary

• The majority of the treatment emergent adverse events were mild to moderate in severity and were ≤ Grade 3
• Treatment emergent serious adverse events were infrequent during the study and mostly respiratory-related
• Pamrevlumab infusions were generally well tolerated, mild to moderate in severity (no serious AEs observed) and did not lead to study discontinuations
• In general, pamrevlumab was well tolerated in IPF and warrants further clinical investigation
STUDY FGCL-3019-079

Open-Label, Single-Arm Phase 2 Study in Non-Ambulatory Subjects with Duchenne Muscular Dystrophy
Study FGCL-3019-079 Design

- An open-label, single-arm Phase 2 study in non-ambulatory DMD patients
- Each subject will receive IV infusions of pamrevlumab (35 mg/kg every 2 weeks, not to exceed 150 cc/hour) for up to 156 weeks
- All subjects are closely monitored for safety

DMD 079- Study (N=21)

- Screening
- Pamrevlumab (35 mg/kg, q2W)
- Follow-up

- Up to 4 weeks
- 156 weeks
- 2 weeks
Key Inclusion Criteria

- At least 12 years of age
- Non-ambulatory
- Brooke Score for Arms and Shoulders ≤5
- Diagnosis of DMD by medical history and confirmed Duchenne mutation in available genetic testing using a validated genetic test
- Able to perform spirometry
- Able to undergo cardiac and extremity (upper arm) MRI
- Percent predicted FVC between 40 and 90, inclusive
- At least one historical FVC% predicted value within 18 months of baseline
- Left ventricular ejection fraction ≥45% as determined by cardiac MRI at screening or within 3 months prior to Day 0
- Patients currently receiving heart failure cardiac medications must achieve a stable regimen for at least 3 months prior to screening
- On a stable dose of corticosteroids for a minimum of 6 months, with no substantial change in dosage for a minimum of 3 months
Key Exclusion Criteria

- Requires ≥16 hours continuous ventilation
- Anticipated spine surgery within 156 weeks
- Severe uncontrolled heart disease including any of the following:
  - Need for IV diuretics or inotropic support within 3 months prior to screening
  - Hospitalization for a heart failure exacerbation or arrhythmia in last 3 months
  - Arrhythmia requiring anti-arrhythmic therapy
- Hospitalization due to respiratory failure in the last 6 weeks
- Poorly controlled asthma or underlying lung disease
- BMI ≥40 kg/m2 or weight >117 kg
- Exposure to another investigational drug or approved product for DMD within 28 days prior to start of study treatment (or 5 half-lives, whichever is longer) with the exception of deflazacort
Status of Study 079

- Enrollment is complete, with 21 subjects currently on study
- 10 U.S. sites
- An interim analysis will be conducted after at least 10 to 12 subjects have completed 52 weeks of treatment
- Summary of patient exposure to pamrevlumab in days:

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<tr>
<th>Site ID</th>
<th>All Subjects (N=21) n (%)</th>
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<tbody>
<tr>
<td>7901</td>
<td>1 (4.8)</td>
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<tr>
<td>7903</td>
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<tr>
<td>7921</td>
<td>1 (4.8)</td>
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<tr>
<td>All Sites</td>
<td>21 (100.0)</td>
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<table>
<thead>
<tr>
<th>Statistics</th>
<th>Study 079 (N=21)</th>
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<tr>
<td>Mean (SD) (days)</td>
<td>326.4 (243.0)</td>
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<tr>
<td>Range (days)</td>
<td>29, 872</td>
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<tr>
<td>PEY* (years)</td>
<td>18.77</td>
</tr>
</tbody>
</table>

*PEY = All patients’ duration on treatment/365.25

- Currently, 16 subjects have been on the study for more than 6 months and 3 subjects >2 years
Summary of Safety

- All subjects are currently on the study
- No death on the study
- 90% of subjects had TEAEs, none of the adverse events led to treatment discontinuation
- All TEAEs were mild to moderate in severity and were graded 1-3 per CTCAE. There were no grade >4 adverse events reported to date
- All vitals and labs were within accepted ranges for patients on the study
QUESTIONS?
Thank you