### Long-term Safety and Efficacy of Pegunigalsidase Alfa Administered Every 4 Weeks in Patients With Fabry Disease: 2-year Interim Results from the Ongoing Phase 3 BRIGHT31 Open-label Extension Study

**Introduction**

- Fabry disease is a rare X-linked disorder caused by deficiency of lysosomal enzyme α-galactosidase A (α-GAL), leading to accumulation of glycocerebrosides, which affect multiple organ systems (skin, heart, kidneys, blood vessels, heart, and nervous system).

### Methods

- **Study Design:**
  - Randomized, open-label, Phase 3 clinical trial (NCT02147169) with 2-year extension (NCT03766596).
  - 283 patients with Fabry disease (mean age 43 years, 87% male).
  - Patients were previously treated with agalsidase beta (AGB) for a mean of 5.1 years (range 0.5–60).
  - Eligibility criteria: ≥18 years, mean eGFR > 60 mL/min/1.73 m², ADAs at baseline.

- **Study Treatment:**
  - Pegunigalsidase alfa (P-UGA) 2 mg/kg by subcutaneous injection every 4 weeks.

- **Efficacy and Safety Endpoints:**
  - Efficacy: Change in eGFR, β2-microglobulin (β2-MG), lysosomal Gb3 (LysoGb3).
  - Safety: Frequency and severity of TEAEs, ADA levels.

### Results

- **Change in eGFR during treatment:**
  - Median annualized eGFR slope was more negative following the switch to P-UGA compared to PAGB (−3.1% vs. −0.5% per year, p < 0.0001).

- **β2-Microglobulin Level:**
  - Mean annualized β2-MG slope was −8.5% vs. −1.4% per year, p < 0.0001.

- **Lysosomal Gb3:**
  - Mean annualized LysoGb3 slope was −13.6% vs. −1.6% per year, p < 0.0001.

### Conclusions

- **Efficacy:**
  - P-UGA significantly improved renal and cardiac function compared to AGB.

- **Safety:**
  - TEAEs were mild to moderate in severity, non-serious, and all resolved or were resolved at the interim analysis (August 2021).

- **ADA Response:**
  - All patients with ADAs were previously treated with AGB and had ADAs at baseline.

### Disclosure

- **Disclosures:**
  - **Author Disclosures:**
    - All authors disclose no financial relationships with commercial entities.
  - **Funding:**
    - The BRIGHT31 study was sponsored by Protalix Biotherapeutics.

---

### Table 1: Patient Characteristics and Demographics at Baseline (n = 290)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Male</th>
<th>Female</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.7</td>
<td>35.3</td>
<td>43.5 (9.2)</td>
</tr>
<tr>
<td>Body mass index (BMI)</td>
<td>30.4</td>
<td>28.8</td>
<td>29.6 (4.1)</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>82.2</td>
<td>76.5</td>
<td>79.3 (11.4)</td>
</tr>
</tbody>
</table>

---

### Table 2: Incidence of Treatment-emergent Adverse Events (n = 290)

<table>
<thead>
<tr>
<th>Event Category</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>All adverse events</td>
<td>1087</td>
<td>54%</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>48</td>
<td>2%</td>
</tr>
<tr>
<td>Serious adverse events related to treatment</td>
<td>2</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

---

### Table 3: Incidence of Serious Adverse Events (n = 290)

<table>
<thead>
<tr>
<th>Event Category</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>All serious adverse events</td>
<td>48</td>
<td>2%</td>
</tr>
<tr>
<td>Serious adverse events related to treatment</td>
<td>2</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

---

### Table 4: Change in eGFR during Treatment (% change from baseline, n = 290)

<table>
<thead>
<tr>
<th>Visit</th>
<th>Mean (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>144 (6)</td>
</tr>
<tr>
<td>Week 108</td>
<td>-13.6 (1.4)</td>
</tr>
</tbody>
</table>

---

### Figure 1: Pegunigalsidase Alfa (2 mg/kg) Concentration Over Time

- **Concentration Profile:**
  - Mean (SE) concentration of pegunigalsidase alfa was 144 ± 6 nM at Week 0, decreasing to 13.6 ± 1.4 nM at Week 108.

---

### Figure 3: Study Inclusion and Exclusion Criteria

- **Criteria for Inclusion:**
  - Patients with Fabry disease ≥18 years of age.
  - Mean eGFR > 60 mL/min/1.73 m².
  - ADAs at baseline.

- **Criteria for Exclusion:**
  - Pregnant or breastfeeding women.
  - Patients with a history of malignant neoplasms.

---

### Figure 5: Change in eGFR During Treatment

- **Change in eGFR:**
  - The median annualized eGFR slope was more negative following the switch to P-UGA compared to PAGB (−3.1% vs. −0.5% per year, p < 0.0001).

---

### Figure 7: Distribution of ADAs Over Time

- **Antibody Distribution:**
  - ADAs were detectable at baseline in 14% of patients, with a median titer of 0.10 (range 0.01–0.87).

---

### References

- Fabry disease is a rare X-linked disorder caused by deficiency of lysosomal enzyme α-galactosidase A (α-GAL), leading to accumulation of glycocerebrosides, which affects multiple organ systems (skin, heart, kidneys, blood vessels, heart, and nervous system).

---

### Author Disclosures

- All authors disclose no financial relationships with commercial entities.