**RESULTS – SAFETY**

- No discontinuations
- No serious adverse events
- AEs to date have generally been mild to moderate in intensity
- No reports of fluid overload
- No consistent AEs yet, except muscle spasms
  - Also observed in prior diabetic CKD trials
  - Present as muscle contraction, usually in the lower extremity, and similar to exercise-induced cramps
  - Usually transient, occurring in first month and resolving a few weeks after initiation is completed
- Not associated with evidence of muscle toxicity as assessed by CKD-ESRD Network

**RESULTS – EFFICACY**

- Clinically meaningful increases in eGFR across multiple subgroups
- Activity in earlier and later stages of disease

**DEMOGRAPHICS AND BASELINE CHARACTERISTICS**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (N=262)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>58.1 ± 11.5</td>
<td></td>
</tr>
<tr>
<td>Sex (male)</td>
<td>54.6%</td>
<td></td>
</tr>
<tr>
<td>Race (White)</td>
<td>18.5%</td>
<td></td>
</tr>
<tr>
<td>BMI (mean)</td>
<td>29.7 ± 5.2</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>54.6%</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>43.1%</td>
<td></td>
</tr>
</tbody>
</table>

**EFFECTS OF BARDOXOLONE Methyl**

- No consistent AEs yet, except muscle spasms
- Muscle spasms: 19.5% (26/134), 87% (23/26)
- No fluid overload
- No consistent AEs yet, except muscle spasms

**BLOOD PRESSURE AND BNP**

- Patients with poorly controlled hypertension (BP > 160/100 mmHg)
- Mean BNP decreased by 11% at Week 12
- No evidence of fluid overload at Week 12

**DISTRIBUTION OF eGFR CHANGES**

All patients demonstrated eGFR increases from baseline
- 87% of patients demonstrated increases of at least 10 ml/min/1.73 m²
- 66% of patients demonstrated increases of at least 10 ml/min/1.73 m²
- 22/20 (72%) of patients had an improvement in CKD stage and none worsened

**SPASMS**

- Muscle spasms: 19.5% (26/134), 87% (23/26)
- No fluid overload
- No consistent AEs yet, except muscle spasms

**DISTRIBUTION OF UACR CHANGES**

All patients demonstrated UACR decreases from baseline
- 40% of patients demonstrated decreases of at least 30% from baseline
- 11% of patients demonstrated no change in UACR

**CONCLUSIONS**

- Phase 2 CARDINAL study demonstrates bardoxolone methyl significantly increases eGFR in patients with Alport syndrome after 12 weeks of treatment
- eGFR increases in CARDINAL were observed across full range of baseline eGFR values (range: 24 to 94 ml/min/1.73 m²) and across multiple subgroups
- Most patients demonstrated improvements in CKD stage
- Increases are similar in magnitude to those previously observed in patients with type 2 diabetes and Stage 3b CKD
- Bardoxolone methyl was well tolerated in patients with Alport syndrome
- No discontinuations from study
- No serious adverse events
- No effect on blood pressure
- When normalized by change in eGFR, urinary protein was unchanged from baseline
- AEs to date have been mild to moderate in intensity
- Muscle spasms were mild to moderate in severity and not associated with evidence of muscle toxicity

**PHASE 3 STUDY**

- Phase 3 PHOENIX trial studying Bard in ADPKD, type 1 diabetic CKD, IgA nephropathy, and FSGS is underway