Hereditary angioedema (HAE) is a rare genetic disease caused by deficiency or dysfunction of the C1 inhibitor, and is characterized by episodes of attacks.

KVD900 is an investigational and placebo-controlled therapy for the treatment of HAE attacks.

KVD900 was evaluated in a phase 2, placebo-controlled, double-blind, crossover trial in patients with HAE experiencing moderate to severe attacks

Given the lack of a "gold standard," several patient-reported outcomes (PROs) were collected to capture the patient experience.

The Patient Global Impression of Change (PGI-C) scale has been used in HAE studies and assesses improvement in overall symptoms. PGI-C has been validated in a number of other episodic diseases against well-established measures.

Cross-tabulations of PGI-C endpoints versus the VAS and PGI-S endpoints were performed to ascertain the relationship between patient scores on the PGI-C scale and other PRO measures in the KVD900 phase 2 trial after the main study results were reported.

### Outcome Measures and Statistical Analyses

<table>
<thead>
<tr>
<th>Measure</th>
<th>Scale/Range</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGI-C</td>
<td>0 to 100</td>
<td>0.87</td>
<td>0.53</td>
<td>0.67</td>
</tr>
<tr>
<td>VAS</td>
<td>0 to 100</td>
<td>0.67</td>
<td>0.53</td>
<td>0.53</td>
</tr>
<tr>
<td>PGI-S</td>
<td>0 to 100</td>
<td>0.67</td>
<td>0.53</td>
<td>0.53</td>
</tr>
</tbody>
</table>

A PGI-C rating of "better" with persistence is more specific but less sensitive than PGI-C rating of "a little better" with persistence. Patients in this phase 2 trial (ClinicalTrials.gov ID: NCT04208412) were adults aged 18 years with HAE type 1 or 2, not on prophylactic therapy, and had experienced ≥3 attacks in the past 90 days.

In this study, an open-label single 600 mg dose of KVD900 was administered to patients in the 3 arms for assessment of 6 pharmacodynamic parameters (Part 1) (Figure 1).

Patients were then randomized to receive 2 300 mg doses of KVD900 at 1-hour intervals in a crossover fashion for 2 weeks to evaluate the following parameters.

- # Patients experiencing attacks eligible for treatment if attacks were mild or moderate in severity and were not associated with the face or tongue, and if they had a sufficient resolving period on demand treatment with ready access to non-invasive on-demand treatment for rescue if the deemed necessary.

This poster presents data from Part 2 of this phase 2 study.

### Conclusions

- The majority of attacks rated a "little better" or higher with persistence achieved "better" or higher with persistence within the assessment period, irrespective of treatment received (KVD900 or placebo) (Figure 4).

PGI-C scoring of "a little better" or higher with persistence had high specificity compared with VAS and PGI-S improvement.

Cohen’s kappa was 0.70 and 0.73 for PGI-C scoring of "better" or higher with persistence compared with KVD900 and placebo composite VAS improvements, indicating moderate and substantial agreement, respectively.

Other conclusions include:

- Moderate to substantial agreement between PGI-C and other PROs suggests that improvement on PGI-C was significant in patients that were significant for the patient perspective.

Acknowledgments

This study was supported by KalVista Pharmaceuticals Ltd. Medical writing assistance was provided under the direction of the authors by Lisa Baker, PhD, and Brittany Eldridge, BSc, of ICON Health Limited, and was supported by KalVista Pharmaceuticals, Inc.

Presented during the 2021 ACAAI Annual Meeting, November 4–8, 2021, New Orleans, LA.

References