Background
- In June 2014, quadrivalent live attenuated influenza vaccine (LAIV4) was preferentially recommended by the US Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) for healthy children aged 2–8 years.
- The recommendation was based on clinical studies demonstrating superior relative efficacy for LAIV compared with inactivated influenza vaccine (IV).
- Due to the reduced effectiveness of LAIV4 against A/H1N1 pdm09 strains in the US during the 2013–2014 and 2015–2016 influenza seasons, the preferential recommendation was removed for the 2015–2016 season, and subsequently the vaccine was not recommended for use in the US for the 2016–2017 and 2017–2018 seasons.
- Clinical and laboratory research indicated that the most probable cause of reduced LAIV effectiveness against A/H1N1 pdm09 strains was poor replicative fitness of the A/California and A/Bolivia H1N1 pdm09 strains in LAIV.
- To address this issue, new assays were used to identify H1N1 LAIV.

Objective
- To compare the shedding and immunogenicity of a new A/H1N1 strain (A/Slovenia), selected using the new assays, to a previous strain (A/Bolivia) with reduced effectiveness.

Methods
- This phase 4, randomized, double-blind, multicenter trial enrolled 200 healthy children aged 24 to <48 months (NCT03143101).
- Children were randomized 1:1:1 to receive two doses of a new H1N1 A/Slovenia strain (LAIV3 2015–2016 or LAIV4 2015–2016 formulations) from Days 4 to 5 after Dose 2.

Results
- Table 1: Baseline demographics and characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>N (n=66)</th>
<th>Mean age, months (SD)</th>
<th>Gender, n (%)</th>
<th>Ethnicity, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAIV3 2015–2016</td>
<td>22 (34)</td>
<td>36.0 (6.4)</td>
<td>17 (26)</td>
<td>7 (11)</td>
</tr>
<tr>
<td>LAIV4 2015–2016</td>
<td>23 (35)</td>
<td>35.0 (6.8)</td>
<td>18 (28)</td>
<td>7 (11)</td>
</tr>
<tr>
<td>All children (n=200)</td>
<td>45</td>
<td>35.3 (6.7)</td>
<td>35 (57)</td>
<td>14 (23)</td>
</tr>
</tbody>
</table>

- The study met its primary endpoint, as H1N1 HA seroconversion rates were higher for LAIV4 containing A/Slovenia than LAIV4 containing A/Bolivia after both Dose 1 and Dose 2 (P=0.006 and P=0.001, respectively) (Figure 2).

Conclusions
- This study met its primary endpoint, demonstrating significantly higher HA seroconversion rates after Dose 1 and Dose 2 for the new H1N1 A/Slovenia strain than for the A/Bolivia strain, which was associated with reduced effectiveness.
- Furthermore, the new H1N1 A/Slovenia strain demonstrated immune responses comparable to a highly efficacious H1N1 LAIV strain.
- Improved immune response with A/Slovenia compared with A/Bolivia is supported by recent UK LAIV data from the 2017–2018 season, where the A/Slovenia strain demonstrated 90% (95% CI: 58–97) effectiveness in 2–17-year-olds against circulating A(H1N1)pdm09 strains.9
- The results of the study validate improvements made to the LAIV strain selection process and support the use of LAIV as a vaccine option, as reflected by the positive ACIP recommendation for the 2018–2019 influenza season in the US.

References