Vamorolone is a first-in-class dissociative steroid engineered to unhook anti-inflammatory effects from glucocorticoid (GC)-mediated adverse effects. Growth delay is a well-recognized adverse effect (AE) associated with traditional GCs, which are the standard-of-care (SOC) for patients with Duchenne muscular dystrophy (DMD).

Results

- **Patients**: Most patients (89.1%) who entered the LTE completed the 2-year treatment period (Figure 1a).
- **Efficacy**: Participants assigned to vamorolone at 2.0 and 6.0 mg/kg/day initial doses showed a mean increase in 30-m Walk Test (TTSTAND) velocity of 0.011 ± 0.2488 (CI: 0.006, 0.0465) after 24 months that was not different from vamorolone 3.0 mg/kg/day baseline (Figure 2a).
- **Safety and tolerability**: Over a 30-month treatment period, at doses of up to 6.0 mg/kg/day, vamorolone appears to be well-tolerated with 89.1% of patients completing the study, and only 1 TEAE leading to discontinuation, and 2 SAE or serious adverse events (SAEs).

Conclusions

- The mean increase in TTSTAND velocity did not decline to below baseline by this time, in keeping with observations with other chronic oral GC-naive DMD patients modified with vamorolone (a 2.5-year delay in decline in function).
- Improved functional improvements were observed in TTCLIMB velocity, TTRW velocity, NSA score total, and 6MWT distance for participants on 2.0 and 6.0 mg/kg/day initial dose after a 30-month treatment period.

Table 1. AEs by dose at time of event

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Time to Event</th>
<th>Event Count</th>
<th>Event Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 mg/kg</td>
<td></td>
<td>1</td>
<td>Pain in extremity</td>
</tr>
<tr>
<td>0.75 mg/kg</td>
<td></td>
<td>4</td>
<td>Vomiting</td>
</tr>
<tr>
<td>1.0 mg/kg</td>
<td></td>
<td>2</td>
<td>Nausea</td>
</tr>
<tr>
<td>2.0 mg/kg</td>
<td></td>
<td>1</td>
<td>Pain in extremity</td>
</tr>
<tr>
<td>4.0 mg/kg</td>
<td></td>
<td>1</td>
<td>Vomiting</td>
</tr>
<tr>
<td>6.0 mg/kg</td>
<td></td>
<td>2</td>
<td>Nausea</td>
</tr>
</tbody>
</table>

Safety and tolerability

- **During the 24-month VBP15-LTE Treatment Period, 46 participants (100%) experienced at least one treatment-emergent AE (TEAE).**
- Ten subjects de-escalated the vamorolone dose from 6.0 mg/kg/day to 2.0 mg/kg/day due to a TEAE of weight increase.
- According to local site AE reporting, 3/39 (7.7%) patients were observed to have a total of 6 clinical Events.
- Mean changes in hematologic, chemistry, lipids, or urine analysis parameters were minimal and clinically unremarkable.
- Mean values for glutamate dehydrogenase and gamma-glutamyl transpeptidase normal across all VBP15-LTE timepoints.

There was no significant difference in changes to mean Body Mass Index (BMI) scores between the vamorolone and Duchenne Natural History Study (DNHS) participants.

Comparison of vamorolone- to GC-treated DNHS participants showed a significant weight increase (2.1% vs 0.2%) in mean height percentile change, with no evidence of growth deceleration in the vamorolone group.

- **Results of an open label long-term extension (LTE) study (VBP15-LTE, NCT03038199) showed ongoing improvement in motor function and a favorable safety profile.**
- **Here we report on the long-term tolerability, and efficacy of vamorolone in boys with DMD who completed the 24-week VBP15-LTE-003 trial and the 24-month VBP15-LTE trial, with a total of up to 30 months of vamorolone treatment.**

Trial participants

- Three consecutive multicenter open clinical trials (VBP15-002/003/004) were conducted by the Cooperative International Neuromuscular Research Group (CINGR).
- A CONSORT Chart is shown (Figure 1).

Figure 1. CONSORT Chart

- **Specializing** in Duchenne and Becker muscular dystrophy, CIGR aims to conduct important clinical research in neuromuscular disorders.

Safety and tolerability

- **Motor function improved from baseline to month 18 and returned to baseline levels at month 24.**
- **Continuous treatment for up to 30 months was not associated with linear growth decline.**
- **Mean change in BMI was not significant different with vamorolone compared to GC-treated DNHS participants.**
- **Over a 30-month treatment period, at doses up to 6.0 mg/kg/day, vamorolone appears to be well-tolerated with 89.1% of patients completing the study, and only 1 TEAE leading to discontinuation, and 2 SAE or serious adverse events (SAEs).**
- **In addition, 10 subjects (24%) down titrated due to weight gain but remained on treatment, and there was no impact on linear growth trajectory observed.**

References