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# Real-World Behavioral Improvements in Patients With Rett Syndrome Treated With Trofinetide: Interim Results of the LOTUS Study

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## DISCLOSURES

LC and LR are employees and stakeholders in Acadia Pharmaceuticals Inc. JD has been a consultant for Acadia Pharmaceuticals Inc., AveXis, Marinus Pharmaceuticals, Neurogene Inc., Orion, Taysha Gene Therapies, and Ultra genyx, and contributed to AnavexLife Sciences and Neuron Pharmaceuticals clinical trials. All consultancies are unrelated to this work and all remuneration has been made to her department.

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## INTRODUCTION

• Rett syndrome (RTT) is a rare neurodevelopmental disorder associated with challenges with social interaction, connection to others, and communication<sup>1</sup>

• Trofinetide is approved for the treatment of RTT in patients aged ≥2 years in the United States and patients aged ≥2 years weighing ≥9 kg in Canada<sup>2,3</sup>

• Trofinetide is disease-specific and improves the core symptoms of RTT, evidenced by improvements on the Rett Syndrome Behaviour Questionnaire (RSBQ) in the trofinetide clinical trial program<sup>4-7</sup>

• Caregivers and clinicians are interested in real-world outcomes of trofinetide among a more diverse sample of individuals than in clinical trials

## OBJECTIVE

• To characterize behavioral improvements with trofinetide in patients with RTT in the real-world setting

## METHODS

### LOTUS Study Design and Population

• LOTUS is an ongoing, phase 4, observational, real-world, prospective, online study involving caregivers of patients prescribed trofinetide under routine clinical care<sup>8</sup>

• LOTUS participation lasts for ≥12 months from trofinetide initiation, with the option to extend participation for an additional 12 months

• Caregivers of any patients who were prescribed trofinetide under routine care are eligible for this study; there are no exclusion criteria

### Relevant Study Assessments

• The Behavioral Improvement Questionnaire (BIQ) is a novel measure that has been adapted from the RSBQ, the top caregiver concerns from the US Natural History Study, and the RTT community list of symptoms in the Voice of the Patient Report<sup>9-11</sup>; it consists of questions soliciting a “yes” or “no” response from caregivers as to whether they observed new and/or maintained improvements following treatment with trofinetide compared with the period before starting trofinetide

• A “yes” answer resulted in the opportunity to identify all areas of improvement from a checklist that included alertness, behavioral problems, breathing irregularities, communication tools, eating/swallowing, grinding teeth, mobility or balance, mood, muscle tone abnormalities, nonverbal communication, purposeful use of hands, repetitive movements, sleep, social interaction/connectedness, verbal communication, and other domains

• The BIQ was assessed monthly for 6 months and every 3 months thereafter

• Data are reported to 12 months since the initiation of trofinetide quarterly

## RESULTS

### Demographics and Baseline Characteristics

• In total, 227 caregivers participated in this follow-up (Table 1)

### Behavioral Improvements

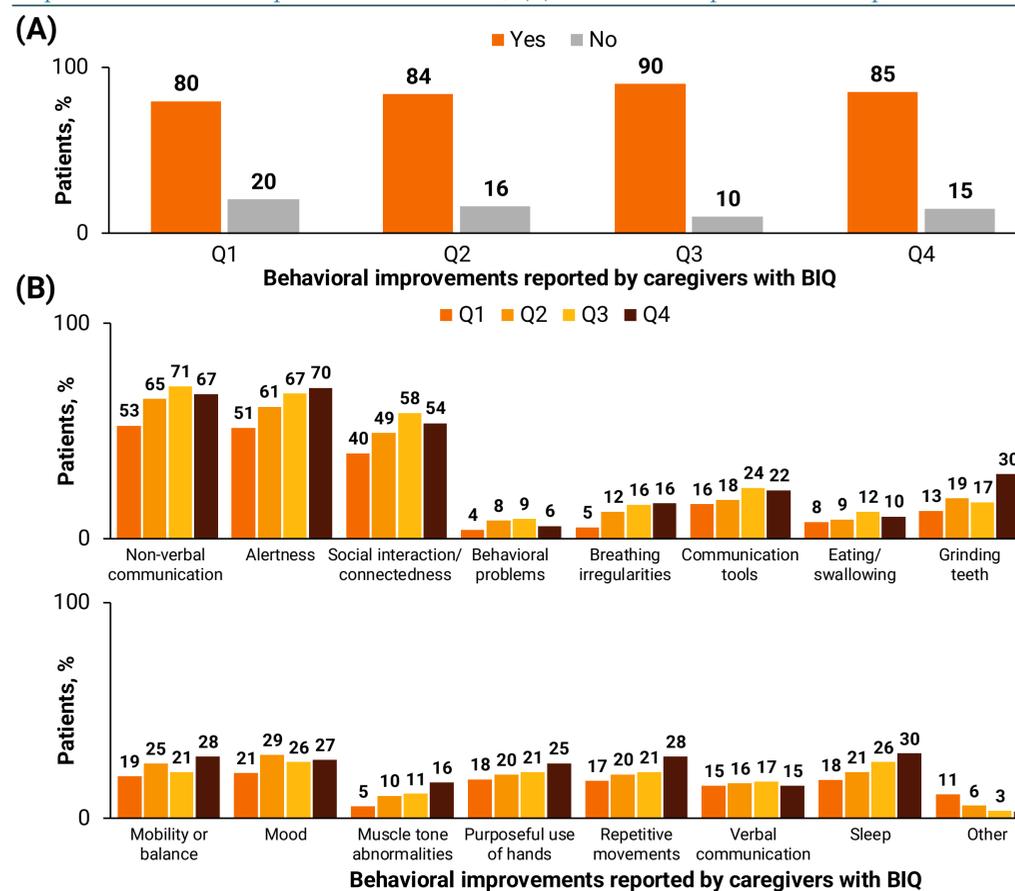
• Overall, 80–90% of caregivers reported behavioral improvements on the BIQ on the first 4 quarters of trofinetide treatment (Figure 1A)

- The most frequently reported improvements were nonverbal communication (53–71%), alertness (51–70%), and social interaction/connectedness (40–58%) (Figure 1B)

• Developmental skills were reported in the “other” category of BIQ (Table 2)

• Most caregivers reported 2–4 new and/or maintained behavioral improvements per month with BIQ

Figure 1. Behavioral Improvements Reported by Caregivers With BIQ. (A) Caregivers Who Reported Behavioral Improvements With BIQ. (B) Behavioral Improvements Reported With BIQ



BIQ, Behavioral Improvement Questionnaire; Q, quarter; RTT, Rett syndrome.

Table 1. Baseline Demographic and Clinical Characteristics

| Characteristic  | LOTUS total (n = 227) |
|---|-----------------------|
| <b>RTT type</b> (n = 206)   |                       |
| Classic   | 134 (65.0)            |
| Atypical  | 57 (27.7)             |
| Does not meet diagnostic criteria for either  | 15 (7.3)              |
| <b>Sex</b> (n = 227)  |                       |
| Male  | 7 (3.1)               |
| Female  | 220 (96.9)            |
| <b>Ethnicity</b> (n = 201)  |                       |
| White   | 162 (80.6)            |
| Black or African American   | 17 (8.5)              |
| Asian   | 10 (5.0)              |
| Other/not disclosed   | 22 (10.9)             |
| <b>Median (IQR) age at time of RTT diagnosis, years</b> (n = 190)                       | 3 (2–5)               |
| <b>Median (IQR) age at time of trofinetide initiation, years</b> (n = 205) <sup>a</sup> | 13 (6–22)             |

Data are n (%) unless stated otherwise.  
<sup>a</sup>Trofinetide initiation is the day of trofinetide shipment.  
IQR, interquartile range; RTT, Rett syndrome.

Table 2. Developmental Milestones Reported in “Other” Category in BIQ

| Domain               | Developmental skill                         | Free-text responses  |
|----------------------|---|--|
| <b>Communication</b> | Used word(s) with meaning                   | <ul style="list-style-type: none"> <li>• “Said mom a few times”</li> <li>• “She try to talk like a baby start to talk she say papa and others things she is improvement little it. She’s starting to progress”</li> </ul>  |
| <b>Fine motor</b>    | Used a fork or spoon to eat with assistance | <ul style="list-style-type: none"> <li>• “When she is eating she can grab the spoon and bring it to her mouth”</li> <li>• “She fed herself with my assistance. Id pierce a piece of fruit like a grape or banana. She would pick up the fork from a plate with her dominant (left) hand and place it in her hand”</li> </ul> |
|                      | Sat without support                         | <ul style="list-style-type: none"> <li>• “She started to sit again unassisted for up to 5 minutes”</li> </ul>  |
|                      | Pulled to standing                          | <ul style="list-style-type: none"> <li>• “Small increase in purposeful movement sitting to standing”</li> </ul>  |
| <b>Gross motor</b>   | Walked independently                        | <ul style="list-style-type: none"> <li>• “Independently walking to the kitchen”</li> </ul>   |
|                      | Climbed up stairs without help              | <ul style="list-style-type: none"> <li>• “Walking up stairs without help”</li> </ul>   |

BIQ, Behavioral Improvement Questionnaire.

## CONCLUSIONS

**The results of LOTUS show that caregivers observe the impact of trofinetide on meaningful functions and behaviors**

- The functions and behaviors include symptoms that are part of the RTT diagnostic criteria, including the loss of hand use, loss of communication skills, and issues with ambulation

**The caregiver-reported behavioral improvements expand on the behavioral improvements observed in trofinetide clinical trials**