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# Assessing Experiences With Trofinetide for Rett Syndrome: Interviews With Caregivers of Participants in Open-label Studies

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# Disclosures

- Kathie M. Bishop **was an employee of Acadia Pharmaceuticals Inc.** while this study was conducted and **owns stocks and stock options in Acadia Pharmaceuticals Inc.**

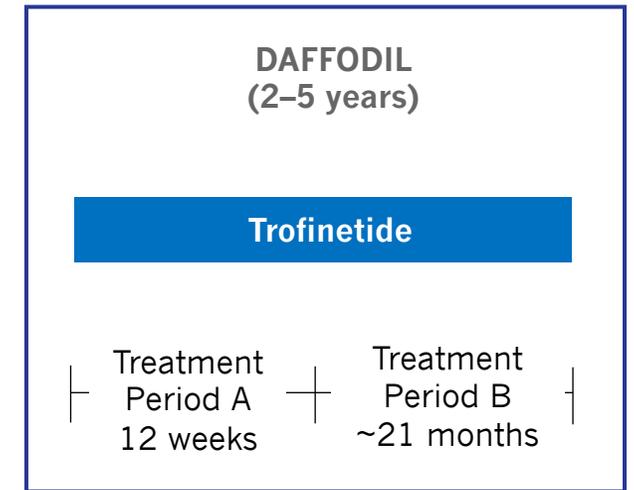
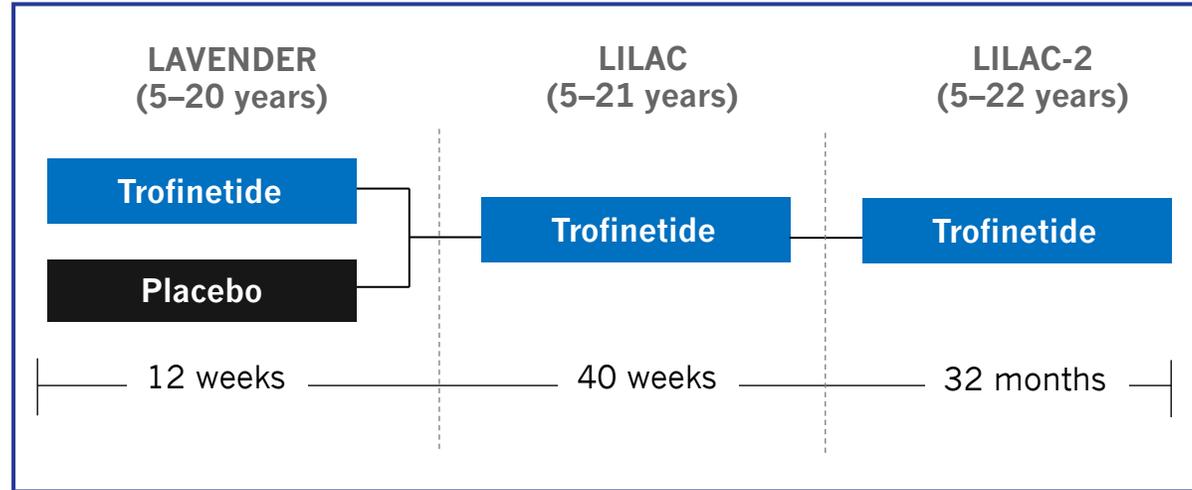
# Introduction

- RTT is a rare neurodevelopmental disorder characterized by loss of verbal communication with limited nonverbal skills, loss of fine and gross motor function, behavioral issues, seizures, hand stereotypies, and gastrointestinal problems<sup>1,2</sup>
- Trofinetide was FDA-approved in March 2023 for the treatment of RTT in adults and pediatric patients aged  $\geq 2$  years<sup>3</sup>
  - Phase 3 study with traditional clinical endpoints – RSBQ and CGI-I – formed the bases for approval
- FDA guidance has emphasized the importance of understanding the patient experience and seeking the patient voice during drug development<sup>8</sup>
- The present study was conducted to gain insight into the patient experience of RTT and trofinetide treatment via interviews with caregivers of participants who completed the trofinetide open label extension clinical studies

CGI-I, Clinical Global Impression–Improvement; RSBQ, Rett Syndrome Behaviour Questionnaire; RTT, Rett syndrome.

1. Neul JL, et al. *Ann Neurol*. 2010;68(6):944–950. 2. Motil KJ, et al. *J Pediatr Gastroenterol Nutr*. 2012;55(3):292–298. 3. DAYBUE (trofinetide) [package insert]. San Diego, CA: Acadia Pharmaceuticals; 2023. 4. Neul JL, et al. *Nat Med*. 2023;29(6):1468–1475. 5. Percy AK, et al. Presented at the 2023 IRSF Rett Syndrome Scientific Meeting, June 5–7, Nashville, TN, USA. 6. Percy AK, et al. Presented at the American Epilepsy Society 2023 Annual Meeting, December 1–5, Orlando, FL, USA. 7. Percy A, et al. *Neurology*. 2023;100:1378 8. US Food and Drug Administration. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-collecting-comprehensive-and-representative-input>. Published June 2018. Accessed October 24, 2023.

# Methods



## Inclusion criteria

- All caregivers of participants who completed the open-label LILAC-2 or DAFFODIL studies were eligible to participate

## Interviews

- Interviews (~60 minutes) focused on participant experiences of RTT, observations of treatment benefit, and meaningfulness of these benefits; no probing of concepts

## Data Analysis

- Interview data assigned thematic codes using an a priori coding framework that was adapted to incorporate emerging themes
- A thematic data analysis approach identified the key themes across interviews

# Caregiver and study participant characteristics

Characteristic	LAVENDER/LILAC/ LILAC-2	DAFFODIL
<b>Caregivers</b>	n=27 <sup>a</sup>	n=7
Sex, n (%)		
Female	24 (88.9)	6 (85.7)
Male	3 (11.1)	1 (14.3)
<b>Study participants with RTT</b>	n=26	n=7
Age, mean (SD) y	12.3 (4.7)	4.5 (0.6)
Age at diagnosis, mean (SD) y	2.7 (1.3)	2.1 (0.7)
Time since diagnosis, mean (SD) y	9.6 (4.7)	2.4 (0.7)

<sup>a</sup>Both parents of 1 study participant took part in an interview simultaneously. For all frequency counts and analyses, information from this interview was handled as 1 caregiver report.

RTT, Rett syndrome; SD, standard deviation.

# Effects of RTT reported by LAVENDER/LILAC/LILAC-2 caregivers

Effects of RTT reported by ≥25% of caregivers, n (%)	LAVENDER/LILAC/LILAC-2 (N=26)
No verbal communication	24 (92.3)
Unable to use hands due to repetitive hand movements	15 (57.7)
Unable to walk	15 (57.7)
Seizures	14 (53.8)
Unable to perform self-care (eg, feeding, brushing teeth, getting dressed)	12 (46.1)
Breathing problems (breath holding or hyperventilating)	9 (34.6)
Mood disturbance (eg, frustrated, anxious, angry, irritable)	8 (30.8)
Constipation	7 (26.9)
Scoliosis	7 (26.9)
Difficulty swallowing	7 (26.9)
Requires feeding tube	7 (26.9)

RTT, Rett syndrome.

# LAVENDER/LILAC/LILAC-2 caregiver-observed improvements with trofinetide

Area/type of improvement with trofinetide use reported by $\geq 15\%$ of caregivers, n (%)	LAVENDER/LILAC/LILAC-2 (N=26)
Engagement with others	11 (42.3)
Hand use	10 (38.5)
Eye gaze	8 (30.8)
Attention/focus/concentration	7 (26.9)
Tobii eye tracker use	7 (26.9)
Ability to make sounds	6 (23.1)
Happier mood or disposition	6 (23.1)
Ability to walk	5 (19.2)
Alertness	5 (19.2)
New words	5 (19.2)
Seizures	4 (15.4)
Aware of environment	4 (15.4)
Repetitive hand movements	4 (15.4)

# LAVENDER/LILAC/LILAC-2 caregiver descriptions of meaningful improvements with trofinetide

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*The biggest thing we noticed was better hand use.*

*I would say just being able to concentrate and not be as upset during activities.... The concentration has made it easier to learn the different material that we've given her.*

*She's totally alert and interested and involved. Like our family parties, that's where my family is like, "Wow, she's really engaged in everything.*

*Her verbalization definitely improved, and she started saying more things.*

*The biggest things we saw were maybe an improvement in her eye gaze. She really became pretty accurate with her Tobii.*

*It was her engagement level with the world outside of her—to me and to friends in school; [it] just blossomed, and it was like a light was turned on.*

”

# Effects of RTT reported by DAFFODIL caregivers

Effects of RTT reported by $\geq 25\%$ of caregivers, n (%)	DAFFODIL (N=7)
No verbal communication	7 (100.0)
Impaired balance	4 (57.1)
Limited ability to use hands	3 (42.9)
Unable to use hands	3 (42.9)
Repetitive hand movements	3 (42.9)
Constipation	3 (42.9)
Unable to sit up	2 (28.6)
Unable to crawl	2 (28.6)
Delayed development of walking ability	2 (28.6)
Poor eye contact	2 (28.6)
Disrupted sleep	2 (28.6)
Unable to feed themselves	2 (28.6)
Irritable or unhappy mood	2 (28.6)

RTT, Rett syndrome.

# DAFFODIL caregiver-observed improvements with trofinetide

Area/type of improvement with trofinetide use reported by ≥15% of caregivers, n (%)	DAFFODIL (N=7)
New words	5 (71.4)
Eye contact	4 (57.1)
Hand use	4 (57.1)
Eye gaze	3 (42.9)
Attention	3 (42.9)
Balance	3 (42.9)
Gross motor skills	3 (42.9)
Response time	2 (28.6)
Tobii eye tracker use	2 (28.6)
Following directions	2 (28.6)
Engagement	2 (28.6)
Awareness	2 (28.6)
Walking	2 (28.6)
Hand movements	2 (28.6)
Fine motor skills	2 (28.6)
Mood or disposition	2 (28.6)

# DAFFODIL caregiver descriptions of meaningful improvements with trofinetide

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*I would say so she both has that better eye gaze with her device and has better eye contact and facial expression.*

*She maintains eye contact. Matter of fact, she uses a lot of that eye contact and concentration. She'll lock you in.*

*Across a lot of motor areas, we've noticed improvement. She's having less falling, better balance. She's more confident with walking.*

*She's less frustrated because she has more success communicating.*

*Her grasp and release has gotten better.*

*It's a huge amount of vocabulary that she has acquired since the trial and more consistent words.*

”

# Common themes of caregiver-observed improvements with trofinetide treatment

Area/type of improvement with trofinetide use reported by >25% of caregivers, n (%)	LILAC/LILAC-2 (n=26)	DAFFODIL (n=7)	Total (N=33)
Hand use	10	4	14 (42.4)
Engaging with others	11	2	13 (39.4)
Eye gaze	8	3	11 (33.3)
Acquired new words	5	5	10 (30.3)
Focusing	7	2	9 (27.3)
Using eye gaze device	7	2	9 (27.3)

# Conclusions

- Caregivers of LAVENDER/LILAC/LILAC-2 and DAFFODIL reported meaningful improvements with trofinetide
  - Positive impact was reported on their child's hand use, engagement with others, eye gaze, attention/focus, ability to say new words, and eye tracker use
- Nearly all caregivers were very satisfied or satisfied with the benefits of trofinetide and reported that their lives and their children's lives were improved with trofinetide treatment
  - In LAVENDER/LILAC/LILAC-2, 24/25 caregivers were very satisfied or satisfied
  - In DAFFODIL, 7/7 caregivers were very satisfied or satisfied
- Future directions include integrating the results of these caregiver exit interviews with clinical trial outcomes