DAYBUE™ treatment management guide for healthcare professionals

The first and only FDA-approved treatment for Rett syndrome (RTT) in adults and pediatric patients 2 years and older.[1,2]

Daybue™ (trofinetide)

Indication

DAYBUE is indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.

Important Safety Information

- **Warnings and Precautions**
  - **Diarrhea:** In a 12-week study and in long-term studies, 85% of patients treated with DAYBUE experienced diarrhea. In those treated with DAYBUE, 49% either had persistent diarrhea or recurrence after resolution despite dose interruptions, reductions, or concomitant antidiarrheal therapy. Diarrhea severity was of mild or moderate severity in 96% of cases. In the 12-week study, antidiarrheal medication was used in 51% of patients treated with DAYBUE.

    Patients should stop taking laxatives before starting DAYBUE. If diarrhea occurs, patients should notify their healthcare provider, consider starting antidiarrheal treatment, and monitor hydration status and increase oral fluids, if needed. Interrupt, reduce dose, or discontinue DAYBUE if severe diarrhea occurs or if dehydration is suspected.

See additional Important Safety Information on page 11.

Please read the full Prescribing Information, also available at DAYBUEhcp.com.

Significant improvements in signs and symptoms of RTT were achieved at Week 12[1]

LAVENDER™ (NCT04181723) was a 12-week, randomized, double-blind, placebo-controlled clinical trial of 187 female patients aged 5-20 years old, designed to evaluate the efficacy and safety of DAYBUE[1,3,a]

	Caregiver completed	Clinician completed
Co-primary endpoints:	• Change from baseline to Week 12 in the **Rett Syndrome Behaviour Questionnaire (RSBQ)** total score[1] • Evaluated changes in their child's signs and symptoms[1,4] • Caregivers used a 0- to 2-point scale to assess 45 symptoms of RTT to determine the RSBQ total score. The maximum possible score is 90[1] • Lower scores reflect lesser severity in signs and symptoms of RTT[1]	• **Clinical Global Impression-Improvement (CGI-I)** score at Week 12[1] • Evaluated whether a patient improved or worsened using a 7-point scale (1=very much improved; 7=very much worse)[5] • A decrease in score indicates improvement[1]
Efficacy results:	Caregivers observed an **almost 3x greater reduction in mean score from baseline** vs placebo in the RSBQ[1] • At Week 12, the LSM change from baseline (SE) was -4.9 (0.94) for DAYBUE and -1.7 (0.90) for placebo, with an LSM placebo-subtracted treatment difference (drug minus placebo) of -3.2 (95% CI: -5.7, -0.6; *P*=0.018).[1] – At baseline, the mean RSBQ total score (SE) was 43.7 (1.21) for DAYBUE and 44.5 (1.26) for placebo[1] – At Week 12, the mean RSBQ total score (SE) was 39.9 (1.38) for DAYBUE and 42.8 (1.42) for placebo[1]	Clinicians observed a **statistically significant improvement** in illness as a whole as measured by the CGI-I with DAYBUE vs placebo[1] • At Week 12, the mean score (SE) was 3.5 (0.08) compared with 3.8 (0.06) for placebo (*P*=0.003)[1] • The LSM placebo-subtracted treatment difference was -0.3 (95% CI: -0.5, -0.1; P=0.003)[1]

At baseline, patients exhibited a range of clinical characteristics, disease severity, and comorbidities.[6]

[a]Patients had a diagnosis of typical Rett syndrome with a documented disease-causing mutation in the *MECP2* gene. Patients were randomized to receive DAYBUE (N=93) or matching placebo (N=94) for 12 weeks.[1]
LSM=least squares mean; SE=standard error.

Important Safety Information (continued)

- **Warnings and Precautions: Weight Loss**
  - In the 12-week study, 12% of patients treated with DAYBUE experienced weight loss of greater than 7% from baseline, compared to 4% of patients who received placebo. In long-term studies, 2.2% of patients discontinued treatment with DAYBUE due to weight loss. Monitor weight and interrupt, reduce dose, or discontinue DAYBUE if significant weight loss occurs.

See additional Important Safety Information on page 11.

Daybue™ (trofinetide)

Demonstrated safety and tolerability profile of DAYBUE[1]

- In controlled and uncontrolled trials in patients with RTT, 260 patients ages 2 to 40 years were treated with DAYBUE, including 109 patients treated for >6 months, 69 patients treated for >1 year, and 4 patients treated for >2 years.[1]

Adverse reactions in at least 5% of patients treated with DAYBUE and at least 2% greater than placebo in the 12-week LAVENDER study were[1]:

Adverse Reactions	DAYBUE (N=93)	Placebo (N=94)
Diarrhea	82%	20%
Vomiting	29%	12%
Fever	9%	4%
Seizure	9%	6%
Anxiety	8%	1%
Decreased appetite	8%	2%
Fatigue	8%	2%
Nasopharyngitis	5%	1%

- **18 patients (19%)** receiving DAYBUE had adverse reactions that led to withdrawal from the study[1]
- The most common adverse reaction leading to discontinuation of treatment with DAYBUE was diarrhea (15%)[1]

In an open-label study in pediatric patients 2 to 4 years of age with RTT, a total of 13 patients received DAYBUE for at least 12 weeks and 9 patients received DAYBUE for at least 6 months. Adverse reactions in pediatric patients 2 to 4 years of age treated with DAYBUE were similar to those reported in LAVENDER.[1]

Important Safety Information

Warnings and Precautions: Weight Loss

- In LAVENDER, 12% of patients treated with DAYBUE experienced weight loss of greater than 7% from baseline, compared to 4% of patients who received placebo[1]
- In long-term studies, 2.2% of patients discontinued treatment with DAYBUE due to weight loss[1]

Monitor weight and, if significant weight loss occurs,

- Interrupt, reduce dose, or discontinue DAYBUE[1]

Daybue™ (trofinetide)

Important Safety Information (continued)

Warnings and Precautions: Diarrhea

- In LAVENDER and in long-term studies, 85% of patients treated with DAYBUE experienced diarrhea[1]
- In those treated with DAYBUE, 49% either had persistent diarrhea or recurrence after resolution despite dose interruptions, reductions, or concomitant antidiarrheal therapy[1]
- In LAVENDER, antidiarrheal medication was used in 51% of patients treated with DAYBUE[1]

In LAVENDER and in long-term studies, the majority of cases of diarrhea were mild to moderate[1]

- **In DAYBUE-treated patients**, 145 of 151 (96%) cases of diarrhea were **mild to moderate** and 6 of 151 (4%) cases were **severe**[7]
- None of the cases of diarrhea were associated with hospitalization[7]
  - Individual patient experience with DAYBUE will vary

Defining mild, moderate, and severe cases of an adverse event[8]:

Mild	Moderate	Severe
Awareness of adverse event but easily tolerated, causing minimal discomfort, and not interfering with normal everyday activities	Sufficiently discomforting to interfere with normal everyday activities	Incapacitating and/or preventing normal everyday activities

For patients with a history of constipation[9]:

70 of 93 DAYBUE-treated patients (75%) in the LAVENDER clinical trial experienced constipation before starting treatment.

Patients experienced diarrhea regardless of previous constipation history.

Daybue™ (trofinetide)

Education and support are key for helping caregivers manage side effects

The management techniques below may help parents and caregivers further prepare for the possibility and methods of addressing diarrhea.

Before starting DAYBUE:

Consider establishing a baseline for bowel activity and fluid status by keeping a log to track stool consistency/frequency for one week prior to starting treatment

Stop use of laxatives[1]

If diarrhea occurs:

Monitor hydration status and increase oral fluids, if needed[1]

Dietary interventions such as administration of fiber supplements may be appropriate[a]

Consider starting antidiarrheal medications such as loperamide (IMODIUM)[1]

[a]Consider fiber supplementation as needed at time of initiation of DAYBUE.

If severe diarrhea or significant weight loss occurs, or dehydration is suspected

- Interrupt, reduce the dosage, or discontinue DAYBUE[1]

Acadia Connect® is a patient and family support program that connects you, your patients, and their family members with dedicated tools and resources. Call Acadia Connect: 1-844-737-2223 Monday through Friday between 8:00AM and 8:00PM ET.

Daybue™ (trofinetide)

Guidance for helping caregivers manage vomiting[a]

Severity of vomiting cases that occurred in LAVENDER[6]

	DAYBUE (N=93)	Placebo (N=94)
Mild n (%)	18 (20%)	8 (9%)
Moderate n (%)	6 (7%)	1 (1%)
Severe n (%)	1 (1%)	0

Defining severity[8]:

Mild: Awareness of adverse event but easily tolerated, causing minimal discomfort, and not interfering with normal everyday activities

Moderate: Sufficiently discomforting to interfere with normal everyday activities

Severe: Incapacitating and/or preventing normal everyday activities

Consider sharing the following information with parents and caregivers caring for a child or adult experiencing vomiting:

To prevent choking, caregivers should sit their child forward or turn their head to the side if vomiting occurs while lying down.[10,11]

When individuals vomit, they can lose water and important salts and become dehydrated. It is important for caregivers to monitor for dehydration.[12]

Signs suggestive of mild dehydration include:

- Dark yellow or brown urine — normal urine should be pale yellow
- Dizziness or light-headedness
- Dry mouth

Signs of severe dehydration include:

- Fewer wet diapers than usual or dark-colored urine
- Dry mouth
- No tears when crying
- Sunken eyes

[a]This guidance was developed by Acadia Pharmaceuticals Inc.

Important Safety Information (continued)

- **Adverse Reactions:** The common adverse reactions (≥5% for DAYBUE-treated patients and at least 2% greater than in placebo) reported in the 12-week study were diarrhea (82% vs 20%), vomiting (29% vs 12%), fever (9% vs 4%), seizure (9% vs 6%), anxiety (8% vs 1%), decreased appetite (8% vs 2%), fatigue (8% vs 2%), and nasopharyngitis (5% vs 1%).

See additional Important Safety Information on page 11.

Daybue™ (trofinetide)

Frequently asked questions (FAQs)

FAQs about diarrhea

Will every patient experience diarrhea?

In LAVENDER and in long-term studies, 85% of patients treated with DAYBUE experienced diarrhea.[1]

Does diarrhea abate over time?

Diarrhea resulting from treatment with DAYBUE may change over time. The implementation of management strategies can help address gastrointestinal issues, but it is important to note that in those treated with DAYBUE, 49% either had persistent diarrhea or recurrence after resolution despite dose interruptions, reductions, or concomitant antidiarrheal therapy.[1]

When did diarrhea first occur in patients?

In the LAVENDER study, diarrhea occurred around 1 week (range of 1–49 days) after starting treatment.[9]

How many treated patients had a history of constipation?

70 of 93 DAYBUE-treated patients (75%) in the clinical trial experienced constipation before starting treatment. Diarrhea was experienced regardless of previous constipation history.[9]

How can caregivers collaborate with others on the care team to manage diarrhea?

Caregivers should inform others on the care team (specialists, therapists, school nurses, teachers) that their child is beginning a treatment with possible gastrointestinal side effects and discuss the management strategies being used at home.

Is diarrhea more severe in patients prescribed a larger weight-based volume of DAYBUE?

For patients taking a larger volume of DAYBUE based on their weight, the frequency of diarrhea was not notably greater than those receiving a lower dose.[9]

FAQs about vomiting

Is it possible to experience both vomiting and diarrhea?

In the clinical trial, 21 of 75 (28%) DAYBUE-treated patients who experienced diarrhea also experienced vomiting.[9]

What if the patient vomits up DAYBUE?

If the patient vomits after taking DAYBUE, instruct the caregiver not to try giving another dose. Instead, they should wait until the next scheduled time to administer DAYBUE.[1]

Important Safety Information (continued)

- **Drug Interactions: Effect of DAYBUE on other Drugs**
  - DAYBUE is a weak CYP3A4 inhibitor; therefore, plasma concentrations of CYP3A4 substrates may be increased if given concomitantly with DAYBUE. Closely monitor when DAYBUE is used in combination with orally administered CYP3A4 sensitive substrates for which a small change in substrate plasma concentration may lead to serious toxicities.

See additional Important Safety Information on page 11.

Daybue™ (trofinetide)

Guidance for managing caregiver expectations around taste[a]

DAYBUE is a pink to red, strawberry-flavored solution that is administered twice daily in volumes ranging from 25 mL to 60 mL, depending on the patient's weight.[1]

The volume of dosage may be a potential challenge or concern, and some patients may be reluctant to take the medication. Consider providing the following tips to help caregivers manage any challenges with taste:

Before administration

1. Caregivers can give their child something cold to numb the taste buds before giving them their medication, eg, ice cream, an ice cube, or ice cold water.[13,14]

During administration

2. Measure amount of medicine accurately first, and then use a medication syringe dipped in sweet syrup[b] and gently squirt the liquid medicine into the side of the cheek or back of the tongue. Do not squirt the medication into the back of the throat as this could cause choking.[13,15]

3. If suitable for their child, caregivers can use play to increase their involvement in taking the medication. For example, pretending to give some medicine to a favorite toy.[13]

4. Playing a favorite piece of music may help reduce both patient and caregiver stress and create a calm environment while giving medication to their child.[16]

After administration

5. Caregivers can give a strong-tasting food or drink after the medication to remove the taste of the medicine.[13]

General tips

6. Caregivers can consider giving the medicine before a favorite activity, so there is a reward afterward.[14]

7. Caregivers should aim to maintain a positive approach when administering the medication and explain to their child that the medicine is to help them feel better.[17]

[a]This guidance was developed by Acadia Pharmaceuticals Inc.
[b]DAYBUE should not be mixed directly with any sweetener.

Important Safety Information (continued)

- **Drug Interactions: Effect of DAYBUE on other Drugs (continued)**
  - Plasma concentrations of OATP1B1 and OATP1B3 substrates may be increased if given concomitantly with DAYBUE. Avoid the concomitant use of DAYBUE with OATP1B1 and OATP1B3 substrates for which a small change in substrate plasma concentration may lead to serious toxicities.

See additional Important Safety Information on page 11.

Daybue™ (trofinetide)

DAYBUE is a twice-daily oral treatment for RTT[1]

DAYBUE is an oral solution (200mg/mL) that is:

Given in the morning and evening, with or without food[1]

Strawberry flavored[1]

For oral administration or via G-tube or G-port of GJ-tube[1]

Recommended Dose for DAYBUE[1]

Patient Weight	DAYBUE Dosage	DAYBUE Volume
9 kg to less than 12 kg	5,000 mg twice daily	25 mL twice daily
12 kg to less than 20 kg	6,000 mg twice daily	30 mL twice daily
20 kg to less than 35 kg	8,000 mg twice daily	40 mL twice daily
35 kg to less than 50 kg	10,000 mg twice daily	50 mL twice daily
50 kg or more	12,000 mg twice daily	60 mL twice daily

Missed dose

If a dose of DAYBUE is missed, the next dose should be taken as scheduled. Doses should not be doubled.[1]

If vomiting occurs after DAYBUE administration, an additional dose should not be taken. Instead, continue with the next scheduled dose.[1]

Storage and handling of DAYBUE

Inform caregivers that DAYBUE should be stored in an upright position and refrigerated at 2°C to 8°C (36°F to 46°F). DAYBUE should not be frozen and must be returned to refrigeration after each dose. **Discard any unused DAYBUE after 14 days of first opening the bottle.** Keep child-resistant cap tightly closed.[1]

GJ=gastrojejunal; G-port=gastrostomy port; G-tube=gastrostomy tube.

Important Safety Information (continued)

- **Use in Specific Population: Renal Impairment**
  - DAYBUE is not recommended for patients with moderate or severe renal impairment.

See additional Important Safety Information on page 11.

Daybue™ (trofinetide)

Support by your patient's side

acadia connect®

Acadia Connect is a patient and family support program that connects you, your patients, and their family members with dedicated tools and resources in the treatment journey after patients have been prescribed DAYBUE (trofinetide).

Acadia Connect offers healthcare providers and practices support services in the following areas:

- Access and coverage support services, including benefits investigations and information to assist with prior authorizations and appeals processes
- Information on appropriate financial assistance options for eligible patients
- Coordination of medication delivery to patients through AnovoRx Specialty Pharmacy
- Support and education throughout the DAYBUE treatment journey

Acadia Connect offers your patients and caregivers support services in the following areas:

- Help to understand and verify insurance coverage
- Information on appropriate financial assistance options
- **Ongoing engagement with educational tools and resources**
- Coordination with AnovoRx Specialty Pharmacy for timely delivery of DAYBUE
- **Support and education throughout the DAYBUE treatment journey**

The Family Access Manager (FAM) offers access support and educational resources to help navigate treatment with DAYBUE, including:

- Insurance coverage education and support
- Information to help resolve access issues for DAYBUE, including information about prior authorizations and appeals processes
- In-person or virtual visits to provide DAYBUE product education
- **Support and education about potential side effects throughout the DAYBUE treatment journey**

Visit AcadiaConnect.com to learn more about our personalized support program, designed to help meet the needs of your patients taking DAYBUE.

Daybue™ (trofinetide)

Indication and Important Safety Information

Indication

DAYBUE is indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.

Important Safety Information

- **Warnings and Precautions**
  - **Diarrhea:** In a 12-week study and in long-term studies, 85% of patients treated with DAYBUE experienced diarrhea. In those treated with DAYBUE, 49% either had persistent diarrhea or recurrence after resolution despite dose interruptions, reductions, or concomitant antidiarrheal therapy Diarrhea severity was of mild or moderate severity in 96% of cases. In the 12-week study, antidiarrheal medication was used in 51% of patients treated with DAYBUE.

    Patients should stop taking laxatives before starting DAYBUE. If diarrhea occurs, patients should notify their healthcare provider, consider starting antidiarrheal treatment, and monitor hydration status and increase oral fluids, if needed. Interrupt, reduce dose, or discontinue DAYBUE if severe diarrhea occurs or if dehydration is suspected.
  - **Weight Loss:** In the 12-week study, 12% of patients treated with DAYBUE experienced weight loss of greater than 7% from baseline, compared to 4% of patients who received placebo. In long-term studies, 2.2% of patients discontinued treatment with DAYBUE due to weight loss. Monitor weight and interrupt, reduce dose, or discontinue DAYBUE if significant weight loss occurs.
- **Adverse Reactions:** The common adverse reactions (≥5% for DAYBUE-treated patients and at least 2% greater than in placebo) reported in the 12-week study were diarrhea (82% vs 20%), vomiting (29% vs 12%), fever (9% vs 4%), seizure (9% vs 6%), anxiety (8% vs 1%), decreased appetite (8% vs 2%), fatigue (8% vs 2%), and nasopharyngitis (5% vs 1%).
- **Drug Interactions: Effect of DAYBUE on other Drugs**
  - DAYBUE is a weak CYP3A4 inhibitor; therefore, plasma concentrations of CYP3A4 substrates may be increased if given concomitantly with DAYBUE. Closely monitor when DAYBUE is used in combination with orally administered CYP3A4 sensitive substrates for which a small change in substrate plasma concentration may lead to serious toxicities.
  - Plasma concentrations of OATP1B1 and OATP1B3 substrates may be increased if given concomitantly with DAYBUE. Avoid the concomitant use of DAYBUE with OATP1B1 and OATP1B3 substrates for which a small change in substrate plasma concentration may lead to serious toxicities.
- **Use in Specific Population: Renal Impairment**
  - DAYBUE is not recommended for patients with moderate or severe renal impairment.

DAYBUE is available as an oral solution (200mg/mL).

Please read the full Prescribing Information, also available at DAYBUEhcp.com.

Daybue™ (trofinetide)

References

1. Acadia Pharmaceuticals Inc. DAYBUE [Package Insert]. San Diego, CA, 2023. **2.** Acadia Pharmaceuticals announces U.S. FDA approval of DAYBUE™ (trofinetide) for the treatment of Rett syndrome in adult and pediatric patients two years of age and older. [press release]. Acadia Pharmaceuticals Inc. March 10, 2023. **3.** Study of trofinetide for the treatment of girls and women with Rett syndrome (LAVENDER™). ClinicalTrials.gov identifier: NCT04181723. Accessed February 9, 2023. https://clinicaltrials.gov/ct2/show/NCT04181723. **4.** Mount RH, Charman T, Hastings RP, et al. The Rett Syndrome Behaviour Questionnaire (RSBQ): refining the behavioural phenotype of Rett syndrome. *J Child Psychol Psyc*. 2002;43(8):1099-1110. **5.** Guy W. ECDEU Assessment Manual for Psychopharmacology, Revised, 1976. US Department of Health, Education, and Welfare. DHEW Publication No. (ADM) 76-338. Accessed January 19, 2023. https://archive.org/details/ecdeuassessmentm1933guyw/mode/1up?ref=ol&view=theater **6.** Acadia Pharmaceuticals Inc. Data on file. ACP-2566-003 Clinical Study Report. 2022. **7.** Acadia Pharmaceuticals Inc. Data on file. ACP-2566-003, -004, -005. Post hoc analyses. 2022. **8.** Acadia Pharmaceuticals Inc. Data on file. ACP-2566-003 Protocol. 2020. **9.** Acadia Pharmaceuticals Inc. Data on file. ACP-2566-003. Post hoc analyses. 2021. **10.** Health Navigator New Zealand. Vomiting in children. Accessed January 19, 2023. https://www.healthnavigator.org.nz/health-a-z/v/vomiting-in-children/ **11.** Agrace. Nausea and vomiting. Accessed January 19, 2023. https://www.agrace.org/findcare/caregiver-education/nausea/ **12.** Health Navigator New Zealand. Dehydration in children and babies. Accessed January 30, 2023. https://www.healthnavigator.org.nz/health-a-z/d/dehydration-children-and-babies/ **13.** Bergene EH, Rø TB, Steinsbekk A. Strategies parents use to give children oral medicine: a qualitative study of online discussion forums. *Scand J Prim Health Care*. 2017;35(2):221–228. **14.** Oxford University Hospitals NHS Trust. Tips to help your child to take medicine. Accessed January 19, 2022. https://www.ouh.nhs.uk/patient-guide/leaflets/files/11990Pmedicine.pdf **15.** Seattle Children's Hospital. Medicine – refusal to take. Accessed January 19, 2022. https://www.seattlechildrens.org/conditions/a-z/medicine-refusal-to-take/ **16.** Chou MY, Chang NW, Chen C, et al. The effectiveness of music therapy for individuals with Rett syndrome and their families. *J Formos Med Assoc*. 2019;118(12):1633–1643. **17.** Great Ormond Street Hospital for Children. Giving your child medicines. Accessed January 19, 2022. https://www.gosh.nhs.uk/medical-information-0/giving-your-child-medicines

Daybue™ (trofinetide)

Help your patients with Rett syndrome get the most out of treatment with DAYBUE

The first and only FDA-approved treatment for Rett syndrome (RTT) in adults and pediatric patients 2 years and older.[1,2]

Proven efficacy[1]
DAYBUE demonstrated statistically significant improvements in the signs and symptoms of RTT compared with placebo, as measured by the mean change from baseline in RSBQ total score and the CGI-I score at Week 12 compared with placebo[1]

Twice-daily dosing[1]
DAYBUE is a strawberry flavored oral solution given in the morning and evening with or without food

Demonstrated safety and tolerability profile[1]
The most common adverse reactions with DAYBUE were diarrhea and vomiting. Tips and strategies are available to help caregivers manage adverse reactions[10,11]

Dedicated support
Acadia Connect provides support for patients and their caregivers, with access, insurance, affordability, and prescription assistance

Learn more about the safety and tolerability of DAYBUE at DAYBUEhcp.com.

Important Safety Information

- **Warnings and Precautions**
  - **Diarrhea:** In a 12-week study and in long-term studies, 85% of patients treated with DAYBUE experienced diarrhea. In those treated with DAYBUE, 49% either had persistent diarrhea or recurrence after resolution despite dose interruptions, reductions, or concomitant antidiarrheal therapy. Diarrhea severity was of mild or moderate severity in 96% of cases. In the 12-week study, antidiarrheal medication was used in 51% of patients treated with DAYBUE.

    Patients should stop taking laxatives before starting DAYBUE. If diarrhea occurs, patients should notify their healthcare provider, consider starting antidiarrheal treatment, and monitor hydration status and increase oral fluids, if needed. Interrupt, reduce dose, or discontinue DAYBUE if severe diarrhea occurs or if dehydration is suspected.

See additional Important Safety Information on page 11.

Please read the full Prescribing Information, also available at DAYBUEhcp.com.

ACADIA

©2023 Acadia Pharmaceuticals Inc. Acadia and Acadia Connect are registered trademarks and DAYBUE is a trademark of Acadia Pharmaceuticals Inc. All other trademarks are the property of their respective owners. All rights reserved. DAY-0066-v2 09/23

Daybue™ (trofinetide)