A Phase 1 Study to Investigate the Safety, Tolerance, Food Effect, Pharmacokinetics and Pharmacodynamics of Single and Multiple Doses of Extended Release Formulations of Centanafadine (CTN) in Young Healthy Subjects

This study has been terminated.

Sponsor:
Neurovance, Inc.

Information provided by (Responsible Party):
Euthymics BioScience, Inc. (Neurovance, Inc.)

ClinicalTrials.gov Identifier:
NCT02827513

First received: July 6, 2016
Last updated: NA
Last verified: July 2016
History: No changes posted

Purpose
The purpose of this study is to investigate the safety, tolerance, food effect, pharmacokinetics (PK) and pharmacodynamics (PD) of single and multiple doses of extended release (XR) formulations of Centanafadine (CTN) in Young Healthy participants.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
</table>
| Adult Attention-deficit Hyperactivity Disorder (ADHD) | Drug: CTN SR1  
Drug: CTN XR1  
Drug: CTN XR2  
Drug: CTN XR3 | Phase 1  |

Study Type: Interventional

Study Design: Allocation: Randomized
Endpoint Classification: Pharmacokinetics/Dynamics Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment
Official Title: A Phase 1 Study to Investigate the Safety, Tolerance, Food Effect, Pharmacokinetics and Pharmacodynamics of Single and Multiple Doses of Extended Release Formulations of Centanafadine (CTN) (Formerly Called EB-1020) in Young Healthy Subjects

Resource links provided by NLM:

MedlinePlus related topics: Attention Deficit Hyperactivity Disorder

U.S. FDA Resources

Further study details as provided by Euthymics BioScience, Inc.:

Primary Outcome Measures:
- Number of participants with treatment emergent adverse events and serious adverse events [Time Frame: Up to approximately 12 days] [Designated as safety issue: No]

Secondary Outcome Measures:
- Maximum observed plasma concentration (Cmax) of Centanafadine (CTN) and metabolite [Time Frame: For Part A: From Day 1 to 12; For Part B: Day 1, Day 2, Day 4, Day 5, Day 6, and Day 7; For Part C: Day 1 to 6] [Designated as safety issue: No]

Blood samples for the determination of plasma concentrations of CTN and metabolite will be collected following dosing as follows: For Part A- on Days 1, 4, 7, and 10 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 18; Days 2, 5, 8, and 11 at hour 24, 30, and 36; Days 3, 6, 9, and 12 at hour 48. For Part B- on Day 1 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 2 at Hour 24/Pre-dose; Day 4 at Pre-dose; Day 5 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 6 at hour 24 and 36; Day 7 at hour 48. For Part C- on Days 1 and 4 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 18; Days 2 and 5 at hour 24, 30, and 36; Days 3 and 6 at hour 48

- Time to maximum plasma concentration (Tmax) of CTN and metabolite [Time Frame: For Part A: From Day 1 to 12; For Part B: Day 1, Day 2, Day 4, Day 5, Day 6, and Day 7; For Part C: Day 1 to 6] [Designated as safety issue: No]

Blood samples for the determination of plasma concentrations of CTN and metabolite will be collected following dosing as follows: For Part A- on Days 1, 4, 7, and 10 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 18; Days 2, 5, 8, and 11 at hour 24, 30, and 36; Days 3, 6, 9, and 12 at hour 48. For Part B- on Day 1 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 2 at Hour 24/Pre-dose; Day 4 at Pre-dose; Day 5 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 6 at hour 24 and 36; Day 7 at hour 48. For Part C- on Days 1 and 4 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 18; Days 2 and 5 at hour 24, 30, and 36; Days 3 and 6 at hour 48

- Area under the plasma concentration-time curve from time zero until the last quantifiable time point (AUC0-last) of CTN and metabolite [Time Frame: For Part A: From Day 1 to 12; For Part B: Day 1, Day 2, Day 4, Day 5, Day 6, and Day 7; For Part C: Day 1 to 6] [Designated as safety issue: No]

Blood samples for the determination of plasma concentrations of CTN and metabolite will be collected following dosing as follows: For Part A- on Days 1, 4, 7, and 10 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 18; Days 2, 5, 8, and 11 at hour 24, 30, and 36; Days 3, 6, 9, and 12 at hour 48. For Part B- on Day 1 at Pre-dose, hour
0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 2 at Hour 24/Pre-dose; Day 4 at Pre-dose; Day 5 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 6 at hour 24 and 36; Day 7 at hour 48. For Part C- on Days 1 and 4 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 18; Days 2 and 5 at hour 24, 30, and 36; Days 3 and 6 at hour 48

- Apparent termination elimination rate constant (kel) of CTN and metabolite [Time Frame: For Part A: From Day 1 to 12; For Part B: Day 1, Day 2, Day 4, Day 5, Day 6, and Day 7; For Part C: Day 1 to 6] [Designated as safety issue: No]

Blood samples for the determination of plasma concentrations of CTN and metabolite will be collected following dosing as follows: For Part A- on Days 1, 4, 7, and 10 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 18; Days 2, 5, 8, and 11 at hour 24, 30, and 36; Days 3, 6, 9, and 12 at hour 48. For Part B- on Day 1 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 2 at Hour 24/Pre-dose; Day 4 at Pre-dose; Day 5 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 6 at hour 24 and 36; Day 7 at hour 48. For Part C- on Days 1 and 4 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 18; Days 2 and 5 at hour 24, 30, and 36; Days 3 and 6 at hour 48

- Apparent terminal elimination half-life (t1/2) of CTN and metabolite [Time Frame: For Part A: From Day 1 to 12; For Part B: Day 1, Day 2, Day 4, Day 5, Day 6, and Day 7; For Part C: Day 1 to 6] [Designated as safety issue: No]

Blood samples for the determination of plasma concentrations of CTN and metabolite will be collected following dosing as follows: For Part A- on Days 1, 4, 7, and 10 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 18; Days 2, 5, 8, and 11 at hour 24, 30, and 36; Days 3, 6, 9, and 12 at hour 48. For Part B- on Day 1 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 2 at Hour 24/Pre-dose; Day 4 at Pre-dose; Day 5 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 6 at hour 24 and 36; Day 7 at hour 48. For Part C- on Days 1 and 4 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 18; Days 2 and 5 at hour 24, 30, and 36; Days 3 and 6 at hour 48

- Last measurable plasma concentration (Clast) of CTN and metabolite [Time Frame: For Part A: From Day 1 to 12; For Part B: Day 1, Day 2, Day 4, Day 5, Day 6, and Day 7; For Part C: Day 1 to 6] [Designated as safety issue: No]

Blood samples for the determination of plasma concentrations of CTN and metabolite will be collected following dosing as follows: For Part A- on Days 1, 4, 7, and 10 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 18; Days 2, 5, 8, and 11 at hour 24, 30, and 36; Days 3, 6, 9, and 12 at hour 48. For Part B- on Day 1 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 2 at Hour 24/Pre-dose; Day 4 at Pre-dose; Day 5 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 6 at hour 24 and 36; Day 7 at hour 48. For Part C- on Days 1 and 4 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 18; Days 2 and 5 at hour 24, 30, and 36; Days 3 and 6 at hour 48

- Area under the plasma concentration-time curve from time zero to infinity (AUC0-inf) from AUC0-last +Clast/kel of CTN and metabolite [Time Frame: For Part A: From Day 1 to 12; For Part B: Day 1, Day 2, Day 4, Day 5, Day 6, and Day 7; For Part C: Day 1 to 6] [Designated as safety issue: No]

Blood samples for the determination of plasma concentrations of CTN and metabolite will be collected following dosing as follows: For Part A- on Days 1, 4, 7, and 10 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 18; Days 2, 5, 8, and 11 at hour 24, 30, and 36; Days 3, 6, 9, and 12 at hour 48. For Part B- on Day 1 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 2 at Hour 24/Pre-dose; Day 4 at Pre-dose; Day 5 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 6 at hour 24 and 36; Day 7 at hour 48. For Part C- on Days 1 and 4 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 18; Days 2 and 5 at hour 24, 30, and 36; Days 3 and 6 at hour 48
• Dose normalized Cmax (Cmax/Dose) of CTN and metabolite [Time Frame: For Part A: From Day 1 to 12; For Part B: Day 1, Day 2, Day 4, Day 5, Day 6, and Day 7; For Part C: Day 1 to 6] [Designated as safety issue: No]

Blood samples for the determination of plasma concentrations of CTN and metabolite will be collected following dosing as follows: For Part A- on Days 1, 4, 7, and 10 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 18; Days 2, 5, 8, and 11 at hour 24, 30, and 36; Days 3, 6, 9, and 12 at hour 48. For Part B- on Day 1 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 2 at Hour 24/Pre-dose; Day 4 at Pre-dose; Day 5 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 6 at hour 24 and 36; Day 7 at hour 48. For Part C- on Days 1 and 4 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 18; Days 2 and 5 at hour 24, 30, and 36; Days 3 and 6 at hour 48.

• Dose normalized AUC (AUC/Dose) of CTN and metabolite [Time Frame: For Part A: From Day 1 to 12; For Part B: Day 1, Day 2, Day 4, Day 5, Day 6, and Day 7; For Part C: Day 1 to 6] [Designated as safety issue: No]

Blood samples for the determination of plasma concentrations of CTN and metabolite will be collected following dosing as follows: For Part A- on Days 1, 4, 7, and 10 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 18; Days 2, 5, 8, and 11 at hour 24, 30, and 36; Days 3, 6, 9, and 12 at hour 48. For Part B- on Day 1 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 2 at Hour 24/Pre-dose; Day 4 at Pre-dose; Day 5 at Pre-dose, hour 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, and 18; Day 6 at hour 24 and 36; Day 7 at hour 48. For Part C- on Days 1 and 4 at Pre-dose, hour 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 18; Days 2 and 5 at hour 24, 30, and 36; Days 3 and 6 at hour 48.

Enrollment: 16

Study Start Date: December 2015

Study Completion Date: January 2016

Primary Completion Date: January 2016 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental: Arm 1</td>
<td>Drug: CTN SR1 Other Name: Centanafadine</td>
</tr>
<tr>
<td>Participants will receive sustained release (SR) Tablet Formulation 1 (SR1) containing 100 mg of Centanafadine (CTN) (2 x 100 mg tablets taken orally by mouth [PO] in the morning at starting at approximately 7 am and 2 x 100 mg tablets PO 5 hours later) for a total daily dose (TTD) of 400 mg on Days 1, 4, 7, and 10.</td>
<td></td>
</tr>
<tr>
<td>Experimental: Arm 2</td>
<td>Drug: CTN XR1 Other Name: Centanafadine</td>
</tr>
<tr>
<td>Participants will receive extended release (XR) Tablet Formulation 1 (XR1) containing 400 mg of CTN (1 x 400 mg tablet PO in the morning) on Days 1, 4, 7, and 10.</td>
<td></td>
</tr>
<tr>
<td>Experimental: Arm 3</td>
<td>Drug: CTN XR2 Other Name: Centanafadine</td>
</tr>
<tr>
<td>Participants will receive XR Tablet Formulation 2 (XR2) containing 400 mg of CTN (1 x 400 mg tablet PO in the morning) on Days 1, 4, 7, and 10.</td>
<td></td>
</tr>
</tbody>
</table>
**Detailed Description:**

The study will be divided into three parts: A, B, C.

**Part A: Single Dose, extended release (XR) Formulation Selection.** This part of the study is a single dose, open label, four-period crossover design in a group of 16 healthy participants.

**Part B: Multiple Ascending Dose.** Part B has been designed to assess the effect of multiple doses of one formulation of XR CTN. This part of the study will be a double-blind, randomized, placebo-controlled design.

**Part C: Food Effect.** Part C has been designed to determine the effect food has on XR CTN. The XR formulation and dose administered will be selected after review of Part B data. This part will be an open-label, two-period crossover design in a group of 16 healthy participants.

**Eligibility**

**Ages Eligible for Study:** 18 Years to 45 Years (Adult)

**Genders Eligible for Study:** Both

**Accepts Healthy Volunteers:** Yes

**Criteria**

**Inclusion Criteria:**

1. Body weight within the normal range for height (body mass index [BMI] between 19.30 kg/m2 inclusive);
2. Negative serum pregnancy test at Screening and negative urine pregnancy test at Day -1 for females of child bearing potential;
3. Women of child-bearing potential must agree to use adequate contraception prior to study entry, for the duration of study participation, and for 90 days following completion of therapy;
4. Be in general good health without clinically significant medical history;
5. Have clinical laboratory test results that are within the laboratory reference range; or if out of range are not clinically relevant and are acceptable to the Investigator and Sponsor medical representative;
6. Negative Human Immunodeficiency Virus (HIV), Hepatitis B and Hepatitis C Screening test;
7. Able and willing to give written informed consent.

**Exclusion Criteria:**

1. Use of any of the following medications will exclude a participant:
   - investigational compound within 30 days prior to Screening;
   - antipsychotic, anxiolytic, or sedative-hypnotic medication within 30 days prior to Screening;
   - any antidepressant medication within 30 days prior to Screening;
   - clonidine within 30 days prior to Screening;
   - cough/cold preparations containing stimulants/sympathomimetic agent within 7 days prior to Day -1;
   - norepinephrine reuptake inhibitors, such as tomoxetine (STRATTERA®) within 30 days prior to Day -1;
   - antihypertensive agents, including diuretics, are not permitted at any time prior to or during the study;
- sedating antihistamines (as a single preparation or in combination) within 7 days prior to Day -1;
- sympathomimetics, appetite suppressants, modafinil, methylphenidate, amphetamine and pemoline within 7 days prior to Day -1;
- Use over the counter medications within 7 days of Investigational Product administration, with the exception of simple analgesics such as paracetamol, oral non-steroidal anti-inflammatory agents and the oral contraceptive pill (if applicable);
- Use of any herbal preparations and melatonin is prohibited and should be discontinued prior to Day -1. The process for discontinuing use of herbal preparations and melatonin prior to Day -1 is at the discretion of the Investigator;

2. A history of, or current evidence for, suicidal ideation, based upon clinical interview and the Columbia Suicide Severity Rating Scale (C-SSRS);

3. A history of known or suspected seizures, spasms, infantile spasms, febrile convulsions, unexplained significant and recent loss of consciousness or history of significant head trauma with loss of consciousness or a family history (first degree relative) of epilepsy or seizures (fits);

4. Subject has a known history of hypertension or Subject has a supine systolic blood pressure (SBP) ≥140 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg. No more than one repeat measurement will be permitted;

5. Subject has a known history of orthostatic hypotension or has an orthostatic blood pressure (BP) drop of ≥20 mm Hg (based on the drop between supine and standing [3 minutes] SBP) at Screening or Day -1;

Note: The eligibility criteria list is not exhaustive.

## Contacts and Locations
Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02827513

### Locations

**Australia**

Melbourne, Australia

### Sponsors and Collaborators

Neurovance, Inc.

### More Information

- **Responsible Party:** Neurovance, Inc.
- **ClinicalTrials.gov Identifier:** NCT02827513  History of Changes
- **Other Study ID Numbers:** NVI-EB1020-105
- **Study First Received:** July 6, 2016
- **Last Updated:** July 6, 2016
- **Health Authority:** Australia: Department of Health and Ageing Therapeutic Goods Administration
Keywords provided by Euthymics BioScience, Inc.:
Centanafadine
Adult attention-deficit hyperactivity disorder
Healthy participants

Additional relevant MeSH terms:
Attention Deficit Disorder with Hyperactivity
Hyperkinesis
Attention Deficit and Disruptive Behavior Disorders
Neurodevelopmental Disorders
Mental Disorders

Dyskinesias
Neurologic Manifestations
Nervous System Diseases
Signs and Symptoms

ClinicalTrials.gov processed this record on July 10, 2016