Chelsea Therapeutics is currently recruiting patients for the first of two pivotal phase III trials designed to demonstrate efficacy and support US marketing approval of the orphan drug droxidopa in symptomatic neurogenic orthostatic hypotension (NOH). This placebo controlled, double-blind study will measure the efficacy of droxidopa on symptoms of orthostatic hypotension in patients with primary autonomic failure (Parkinson’s Disease, Multiple System Atrophy, Pure Autonomic Failure), dopamine beta hydroxylase deficiency and non-diabetic neuropathy.

Systolic blood pressure is transiently and minimally decreased in healthy individuals upon standing. Normal physiologic feedback mechanisms work through neurally-mediated pathways to maintain the standing blood pressure, and thus maintain adequate cerebral perfusion. The compensatory mechanisms that regulate blood pressure upon standing are dysfunctional in subjects with orthostatic hypotension (OH), a condition that may lead to inadequate cerebral perfusion with accompanying symptoms of syncope, dizziness or lightheadedness, unsteadiness and blurred or impaired vision, among other symptoms.

The exact mechanism of action of droxidopa in the treatment of symptomatic NOH has not been precisely defined; however, its norepinephrine replenishing properties with concomitant recovery of decreased noradrenergic activity are considered to be of major importance. By replenishing depleted norepinephrine, droxidopa allows for re-uptake of norepinephrine into peripheral nervous system neurons – stimulating receptors for vasoconstriction and providing physiological improvement in symptomatic neurogenic orthostatic hypotension patients.

Orthostatic hypotension may be a severely disabling condition which can seriously interfere with the quality of life of afflicted subjects. Currently available therapeutic options (Midodrine, fludrocortisone, methylphenidate, ephedrine, indomethacin and dihydroergotamine) provide some symptomatic relief in a subset of subjects, but are relatively ineffective and are often accompanied by severe side effects that limit their usefulness. Only midodrine is specifically approved for this indication. The limitations of these currently available therapeutic options, and the incapacitating nature and often progressive downhill course of disease, point to the need for an improved therapeutic alternative.

Droxidopa was originally developed in Japan by Sumitomo Pharmaceuticals Co., Limited, where it has been approved for use since 1989. Droxidopa has been shown to improve symptoms of orthostatic hypotension that result from a variety of conditions including Parkinson’s Disease, Shy Drager syndrome (Multiple System Atrophy) and Pure Autonomic Failure.

Data from clinical studies and post-marketing surveillance programs conducted in Japan show that the most commonly reported adverse drug reactions with droxidopa are increased blood pressure, nausea, and headache. In clinical studies, the prevalence and severity of droxidopa adverse effects appear to be similar to those reported by the placebo control arm.

More information may be found on the study’s page:

http://clinicaltrials.gov/ct2/show/NCT00633880
Criteria

Inclusion Criteria

- Diagnosis of orthostatic hypotension associated with:
  - Primary Autonomic Failure (Parkinson’s Disease, Multiple System Atrophy, Pure Autonomic Failure)
  - Dopamine Beta Hydroxylase Deficiency
  - Non-Diabetic Autonomic Neuropathy
- A documented fall in systolic blood pressure or in diastolic blood pressure within 3 min of standing
- Provide written informed consent to participate in the study

Main Exclusion Criteria

- Taking ephedrine or midodrine;
- Patients taking ephedrine or midodrine must stop taking these drugs at least 2 days prior to their baseline visit (Visit 2);
- Taking anti-hypertensive medication;
  - The use of short-acting anti-hypertensive medications at bedtime is permitted
- Have a history of more than moderate alcohol consumption;
- Women who are pregnant or lactating;
- Have a history of closed angle glaucoma;
- Have pre-existing sustained severe hypertension (BP ≥ 180/110 mmHg in the sitting position);
- Have atrial fibrillation or, in the investigator’s opinion, have any other significant cardiac arrhythmia;
- In the investigator’s opinion, have any other significant systemic, hepatic, cardiac or renal illness;
- Have diabetes mellitus or insipidus;
- Have a known or suspected malignancy;
- Have known gastrointestinal illness or other gastrointestinal disorder that may, in the investigator’s opinion, affect the absorption of study drug;
- In the investigator’s opinion, have clinically significant abnormalities on clinical examination or laboratory testing;
- Have a serum creatinine level > 130 µmol/L;

3-Month Extension

Patients are eligible to enroll in a 3-month (renewable) safety extension study following completion of trial

Principal Investigators

Horacio Kaufmann, MD       New York University Medical Center
Christopher J Mathias, MD      Imperial School of Medicine

Study Countries

This study is being conducted in the following countries:

- US
- Canada
- UK
- Poland
- Australia

Please refer to the list on the following pages for an active site near you.
**United States Sites**

**Arizona**

**Dedicated Clinical Research**
Litchfield Park, Arizona, United States, 85340
Contact: Jeremy Grove (623) 583-2599 jgrove@dedicatedcr.com
Contact: Kelli Bingham (623) 583-2599 kbingham@dedicatedcr.com
Principal Investigator: Troy Anderson, MD

**Sun Health Research Institute**
Sun City, Arizona, United States, 85351
Contact: Sanja Obradov (623) 876-5468 sanja.obradov@sunhealth.org
Contact: Carolyn Liebsack (623) 875-6514 carolyn.liebsack@sunhealth.org
Principal Investigator: Holly Shill, MD

**California**

**The Parkinson's Institute**
Sunnyvale, California, United States, 94085
Contact: Julie Bergman (408) 542-5626 jbergman@thepi.org
Principal Investigator: Grace Liang, MD

**Pacific Neuroscience Medical Group**
Oxnard, California, United States, 93030
Contact: Juanita Young (805) 278-4148 juanita.young@pacificneuroscience.com
Contact: Jason Fajardo (805) 278-4148 jason.fajardo@pacificneuroscience.com
Principal Investigator: James Sutton, MD

**Florida**

**Southeastern Integrated Medical**
Gainesville, Florida, United States, 32607
Contact: Judy West (352) 333-3885 research@simedpl.com
Contact: Tracy Terry (352) 333-3885 research@simedpl.com
Principal Investigator: Anne Rottmann, MD

**University of Miami Miller School of Medicine**
Miami, Florida, United States, 33136
Contact: Donald Koggan (305) 243-7424 dkoggan@med.miami.edu
Contact: Julie Steele (305) 243-7526 jsteele@med.miami.edu
Principal Investigator: Khema Sharma, MD

**Mayo Jacksonville Dept of Neurology**
Jacksonville, Florida, United States, 32224
Contact: Francine Parfitt (904) 953-0109 parfitt.francine@mayo.edu
Principal Investigator: William Cheshire, MD

**Illinois**

**North Chicago VA Medical Center**
North Chicago, Illinois, United States, 60064
Contact: Deborah Zeedyk (224) 610-1311 deborah.zeedyk@va.gov
Principal Investigator: Janice Gilden, MD

**Saint Mary of Nazareth Hospital Center**
Chicago, Illinois, United States, 60622
Contact: Maria Cubias (312) 770-3455 mcub25@yahoo.com
Principal Investigator: Janice Gilden, MD

For an up to date list please refer to the study page at: [http://clinicaltrials.gov/ct2/show/NCT00633880?show_locs=Y#locn](http://clinicaltrials.gov/ct2/show/NCT00633880?show_locs=Y#locn)
United States Sites

Indiana

**Indiana Medical Research, LLC**
Elkhart, Indiana, United States, 46514
Recruiting

Contact: Sheri Hapner (574) 296-3903 shapner@elkhartclinic.com
Contact: Jami Ludington (574) 296-3905 jludingt@elkhartclinic.com
Principal Investigator: Thomas Vidic, MD

**Kansas City Bone and Joint, PA**
Overland Park, Kansas, United States, 66211
Recruiting

Contact: Jessica Staggs (913) 381-5225 x 468 jstaggs@kcbj.com
Contact: Atul Patel, MD (913) 381-5225 apatel@kcbj.com
Principal Investigator: Atul Patel, MD

Kentucky

**University of Louisville**
Louisville, Kentucky, United States, 40202
Pending

Contact: Kathleen Sheeley (502) 561-3030 kashee01@louisville.edu
Principal Investigator: Irene Litvan, MD

Massachusetts

**Beth Israel Deaconess Medical Center**
Boston, Massachusetts, United States, 02215
Recruiting

Contact: Laura Colburn (617) 632-0899 ldcolburn@bidmc.harvard.edu
Principal Investigator: Roy Freeman, MB

**University of Massachusetts Worcester**
Worcester, Massachusetts, United States, 01655
Recruiting

Contact: Arlene Williams (508) 856-5243 arlene.williams@umassmed.edu
Principal Investigator: Peter Novak, MD, PhD

Maryland

**University of Maryland Hospital**
Baltimore, Maryland, United States, 21201
Pending

Contact: Ine Saka (410) 328-3333 isaka@som.umaryland.edu
Contact: Michelle Cines (410) 328-0157 mcines@som.umaryland.edu
Principal Investigator: Stephen Reich, MD

Michigan

**Henry Ford Health System**
Southfield, Michigan, United States, 48034
Recruiting

Contact: Patricia Kaminski (248) 355-2452 x 25 patriciaakaminski1@yahoo.com
Principal Investigator: Peter Lewitt, MD

Minnesota

**Mayo Clinic Rochester**
Rochester, Minnesota, United States, 55905
Recruiting

Contact: Anita Zeller (507) 266-9033 zeller.anita@mayo.edu
Principal Investigator: Philip Low, MD

New Jersey

**JFK Medical Center**
Edison, New Jersey, United States, 08818
Recruiting

Contact: Albert Obiozo, MD (732) 321-7000 x 8897 aobiozo@solarishes.org
Principal Investigator: Phillip Hanna, MD
Sub-Investigator: Michael Rosenberg, MD

For an up to date list please refer to the study page at: [http://clinicaltrials.gov/ct2/show/NCT00633880?show_locs=Y#locn](http://clinicaltrials.gov/ct2/show/NCT00633880?show_locs=Y#locn)
New York

Columbia University Neurological Institute of NY
New York City, New York, United States, 10032
Contact: Darlene Vecchio (212) 305-1516 dv2009@columbia.edu
Principal Investigator: Louis Weimer, MD

University of Rochester
Rochester, New York, United States, 14618
Contact: Debra Berry (585) 341-7514 debra.berry@ctcc.Rochester.edu
Principal Investigator: Roger Kurlan, MD

NYU Medical Center
New York City, New York, United States, 10016
Contact: Lucy Norcliffe-Kaufmann, PhD (212) 263-7225 lucy.norcliffe-kaufmann@nyumc.org
Principal Investigator: Horacio Kaufmann, MD

Ohio

University Hospitals Case Medical Center
Cleveland, Ohio, United States, 44106
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Contact: Elizabeth Heller (216) 844-7622 elizabeth.heller@uhhospitals.org
Principal Investigator: Thomas Chelimsky, MD

Cleveland Clinic
Cleveland, Ohio, United States, 44195
Contact: Raquel Rozich (216) 444-4959 roziechr@ccf.org
Principal Investigator: Fetnat Fouad-Tarazi, MD

Oklahoma

COR Clinical Research, LLC
Oklahoma City, Oklahoma, United States, 73103
Contact: Lacey Bixler (405) 272-8481 lbixler@corclinical.com
Principal Investigator: Clinton Corder, MD

Tennessee

Vanderbilt University
Nashville, Tennessee, United States, 37212
Contact: Cheri Stewart (615) 322-1880 cheri.stewart@vanderbilt.edu
Principal Investigator: Italo Biaggioni, MD

Texas

UT Southwestern Medical Center
Dallas, Texas, United States, 75390-9036
Contact: Nina Gorham (214) 648-0462 nina.gorham@utsouthwestern.edu
Principal Investigator: Steven Vernino, MD

For an up to date list please refer to the study page at: http://clinicaltrials.gov/ct2/show/NCT00633880?show_loc=US
International Sites

Canada

**Quebec Memory and Motor Skills Disorders Clinic**
Quebec City, Quebec, Canada, G1R 3X5
Contact: Louise Rheaume (418) 692-2227 psa@riq.qc.ca
Contact: Genevieve Roy (418) 692-2227 psa@riq.qc.ca
Principal Investigator: Emmanuelle Pourcher, MD

**SMBD Jewish General Hospital**
Montreal, Quebec, Canada, H3T 1E2
Contact: Julie Benoit (514) 340-8222 x 3525 autonomiclab@jgh.mcgill.ca
Principal Investigator: Ronald Schondorf, MD

**Parkinson's & Neurodegenerative Disorders Clinic**
Ottawa, Ontario, Canada, K1G4G3
Contact: Neila Mendis, MD (613) 737-4440 nmendis@rogers.com
Principal Investigator: Tilak Mendis, MD

**Centre for Movement Disorders**
Markham, Ontario, Canada, L6B1C9
Contact: Susie Oxenham (905) 472-7082 soxenham@movementdisorders.ca
Principal Investigator: Mark Guttman, MD

**McMaster University**
Hamilton, Ontario, Canada, L8L 2X2
Contact: Wendy Meyer (905) 527-4322 x 44506 meyerw@hhsc.ca
Contact: Victoria Malcom (905) 527-4322 x 44506 malcomv@hhsc.ca
Principal Investigator: Carlos Morillo, MD

For an up to date list please refer to the study page at: [http://clinicaltrials.gov/ct2/show/NCT00633880?show_locs=Y#locn](http://clinicaltrials.gov/ct2/show/NCT00633880?show_locs=Y#locn)