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Active, not recruiting

Efficacy and Safety of Endoxifen in Bipolar I Disorder Patients

ClinicalTrials.gov ID NCT06608641

Sponsor Jina Pharmaceuticals Inc.

Information provided by Jina Pharmaceuticals Inc. (Responsible Party)

Last Update Posted 2025-03-17

Study Details Tab

Study Overview

Brief Summary

Bipolar disorder (BPD) is a chronic debilitating illness characterized by drastic swings in mood, energy and functional ability that affects the adult population. Endoxifen is an active metabolite of the marketed drug Tamoxifen and the present study aims to evaluate the efficacy and safety of 8 mg endoxifen in the Bipolar I disorder patient population compared to a placebo arm. Endoxifen will be compared to a placebo to demonstrate that the test product is active and to establish that the study is sufficiently sensitive to detect differences between the investigational products. Thus, Endoxifen will be compared to placebo to demonstrate that the test product is safe and active.

Detailed Description

Protein Kinase C (PKC) plays a major role in the regulation of both pre and postsynaptic neurotransmission. Excessive activation of PKC results in symptoms related to bipolar disorder. PKC exists as a family of closely related subspecies, has a heterogeneous distribution in the brain (with particularly high levels in presynaptic nerve terminals), and plays a crucial role in the regulation of

Feedback

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neuronal excitability, neurotransmitter release, regulation of synaptic plasticity and various forms of learning and memory. Research findings show that the PKC pathway can be used as a target for developing treatment strategies for bipolar disorder. Endoxifen exhibited activity in inhibiting the PKC activity.

In patients with acute bipolar mania, rapid reduction of symptoms is a key treatment goal; however, there is also a need for effective maintenance of effect treatment beyond the period of acute stabilization. The current study will evaluate the efficacy and safety of Endoxifen in Bipolar I Disorder patients against a control placebo arm.

Official Title

A Double-blind, Oral, Multiple-dose, Parallel, Randomized Study to Evaluate Efficacy and Safety of Endoxifen in Bipolar I Disorder Patients With Acute Mania Episodes With or Without Mixed Features

Conditions

Bipolar 1 Disorder

Intervention / Treatment

- Drug: Endoxifen enteric-coated tablet (8 mg)
- Drug: Placebo Tablets

Other Study ID Numbers

Study Start (Actual)

2024-03-19

Primary Completion (Estimated)

2025-06

Study Completion (Estimated)

2025-12

Enrollment (Estimated)

490

Study Type

Interventional

Phase

Phase 3

Resource links provided by the National Library of Medicine

Genetic and Rare Diseases Information Center (https://rarediseases.info.nih.gov/gard) resources: Acute Graft Versus Host Disease (https://rarediseases.info.nih.gov/diseases/6544/acute-graft-versus-host-disease)

FDA Drug and Device Resources (https://clinicaltrials.gov/fda-links)

Contacts and Locations

This section provides contact details for people who can answer questions about joining this study, and information on where this study is taking place.

To learn more, please see the Contacts and Locations section in How to Read a Study Record (https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations).

This study has 12 locations

United States

California Locations

- **Cerritos, California, United States, 90703**
  Synexus
- **Los Angeles,, California, United States, 90015**
  NRC Research Institute
- **Orange, California, United States, 92868**
  NRC Research Institute

Florida Locations

- **Miami Lakes, Florida, United States, 33016**
  Innovative Clinical Research, Inc.
- **Miami Springs, Florida, United States, 33166**
  South Florida Research Phase I-IV, Inc.
- **Miami, Florida, United States, 33165**
  Medical Research of Westchester, Inc.
- **Miami, Florida, United States, 33186**

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Sunshine Medical Research Studies Inc.

Tampa, Florida, United States, 33615
Santos Research Center, CORP

Georgia Locations

East Point,, Georgia, United States, 30344
Accelerated Clinical Trials, LLC

Norcross, Georgia, United States, 30092
Accelerated Clinical Trials, LLC

Peachtree Corners,, Georgia, United States, 30071
Accelerated Clinical Trials, LLC

Mississippi Locations

Flowood, Mississippi, United States, 39232
Precise Research Centers

Participation Criteria

Researchers look for people who fit a certain description, called eligibility criteria. Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read Learn About Studies (https://clinicaltrials.gov/study-basics/learn-about-studies).

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Eligibility Criteria

Description

Inclusion Criteria:

1. Male ≥18 to ≤65 years of age and postmenopausal female patients (12 months with no menses without an alternative medical cause) willing to give written informed consent along with at least one first degree relative (the legally acceptable representative [LAR]) to participate in the study before initiating any study related procedures.
2. Six months of spontaneous amenorrhea with serum FSH levels >40 mIU/mL; OR have had surgical bilateral oophorectomy (with or without hysterectomy) at least six months ago. In the case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment if she is considered not of child-bearing potential.
3. Patients must have a diagnosis of bipolar I disorder and currently display an acute manic episode with or without mixed features according to DSM-5 criteria as judged by the Investigator.
4. Young Mania Rating Scale (YMRS) total score of > 25 and ≥4 on two of four core items (irritability, speech, content, disruptive/aggressive behavior) at screening and at randomization (baseline). The optimal YMRS23 severity threshold of 25 was chosen as this corresponds to a Positive Predictive Value (PPV) of 83%, signifying that 83% of patients with a baseline score ≥ 25 are at least "Markedly ill".
5. Score of >4 in Severity of illness criteria of Clinical Global Impressions- bipolar disorder (CGI-BP) Scale for overall illness at screening and at randomization (baseline).
6. Ready for voluntary hospitalization (along with the accompanying LAR if required and as advised by the Investigator) for the current manic episode for a minimum of 2 days prior to randomization through 21 days of in-patient treatment period.
7. Last intake of the medication(s) for BPD should be 2-7 days prior to randomization depending upon the individual drug's plasma half-life.
8. Patient and / or LAR understand and agree to comply with all the study requirements.
9. Male patients of child begetting potential must be practicing adequate contraception, and any female partners must agree to the use of, highly effective contraception. Documentation should be provided for surgical sterilization for male patients not of child begetting potential.

11. Patient has not taken and agrees not to take any medication or therapy prohibited by the protocol (refer to listing in Section 14.7) for the entire study period.

12. Patients not having any significant diseases or clinically significant abnormal findings except BPD during screening-including medical history, physical examination, laboratory evaluations, 12-lead ECG and X-ray chest (postero- anterior view) recording, etc. which is likely to adversely affect patient's safety and may impact the clinical outcome of the study by participating in the study or study objectives in Investigator's opinion.

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13. Subjects judged clinically not to be at serious suicide risk, (all responses to the Baseline C-SSRS as "No"), or homicidal risk per clinical questioning.

Exclusion Criteria:

1. Newly diagnosed patients not having any suitable treatment exposure in the past for their bipolar mood disorder.
2. ≥ 20% improvement in YMRS total scores between screening and randomization visits.
3. Patients who meet DSM-5criteria for any psychiatric disorder other than Bipolar I Disorder with Acute manic episodes with or without mixed features
4. Patients with seizure disorder
5. Obsessive compulsive disorder or any other co-morbid Axis I anxiety disorder
6. Patients with borderline or anti-social personality disorder of sufficient current severity to interfere with conduct of the study
7. Patients with classical premenopausal symptoms were found at risk of developing intolerable hot flushes, irregular vaginal bleeding.
8. Use of the following medications:
    - Antihypertensive agents if stable dose has not been administered for at least 1 month before randomization
    - Antidepressants in the week (or a period of 5 half-lives of the drug) prior to randomization
    - Continuous daily or standing orders use of benzodiazepines during the month preceding screening (approximately 5 weeks prior to screening)
    - Potent cytochrome P450 (CYP) inducers and CYP2D6/CYP3A4 inhibitors 14 days prior to randomization
    - Depot antipsychotic medications within 1 dosing interval prior to randomization
    - Use of systemic estrogens 6 weeks prior to randomization
    - Patients currently on carbapenem agents
9. Any of the following laboratory abnormalities
    - Serum bilirubin ≥ 1.5 times ULN
    - Serum AST/ALT ≥ 2.5 times ULN
    - Serum TSH >10% above the ULN, regardless of treatment for hypothyroidism or hyperthyroidism
    - Serum triglyceride level > 2.5 times ULN
10. Patients with the following cardiac conditions are excluded:
    - Recent myocardial infarction (<12 months)
    - QTc prolongation (screening electrocardiogram with QTc > 450 msec for men, QTc > 470 msec for women)
    - History of QTc prolongation or using concomitant medications (as judged by the Investigator) which prolong QTc interval

- Sustained cardiac arrhythmia or history of sustained cardiac arrhythmia
- Decompensatory congestive heart failure
- Complete left bundle branch block
- First-degree heart block with PR interval > 0.22 seconds

11. Presence of a coagulation disorder; active or past history of venous thromboembolism including deep venous thrombosis or pulmonary embolism
12. Current prolonged immobilization
13. History or current presence of retinal pathology including retinal vein thrombosis
14. Increased risk of stroke as per the Investigator's discretion
15. History of hypersensitivity or intolerance to tamoxifen, or any other ingredients of the preparation
16. Serious, unstable illnesses including hepatic, renal, gastroenterological, respiratory, cardiovascular (including ischemic heart disease), endocrinologic, neurologic, immunologic, or hematologic disease as per history and medical examination.
17. Drug screen positive for any drug of abuse at screening, (except for benzodiazepines used in therapeutic dose for management of acute mania), active substance abuse in the past 2 months or history of substance dependence (excluding nicotine and caffeine) within 3 months of screening.
18. History of breast or uterine cancer, or abnormal uterine bleeding.
19. Current leukopenia or thrombocytopenia as judged by the Investigator in the best health interest of the subject.
20. Clinically significant suicidal (subject responds "Yes" to any category for Baseline C-SSRS) or homicidal ideation per clinical questioning.
21. Participation in a clinical trial of another investigational drug within 30 days prior to screening.

Ages Eligible for Study

18 Years to 65 Years (Adult, Older Adult)

Sexes Eligible for Study

All

Accepts Healthy Volunteers

No

Study Plan

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This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose : Treatment
Allocation : Randomized
Interventional Model : Parallel Assignment
Masking : Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Masking Description: All subjects, investigators and research staff will be blinded to the treatment allocation. Only personnel who are not involved in the interpretation and analysis of the study data will be allowed access to the blinded information

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Endoxifen Arm Endoxifen enteric-coated tablet (8 mg). Patients will continue treatment with their initial randomized medication for 3 weeks	Drug: Endoxifen enteric-coated tablet (8 mg) • Patients will continue treatment with their initial randomized medication for 3 weeks
Placebo Comparator: Placebo Arm Placebo tablets. Patients will continue administration with their initial randomized medication for 3 weeks	Drug: Placebo Tablets • Patients will be treated with Endoxifen Placebo Tablets for 21 days

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Efficacy - mean change from baseline to Day 21 in the total YMRS score	Primary efficacy endpoint will be the mean change from baseline to Day 21 in the total YMRS score. The point estimate and 95% confidence interval for the mean change from Day 0 (baseline) to Day 21 in total YMRS score for the difference between test and placebo control treatment will be computed and reported for mITT set. Superiority of test over placebo will be claimed if 95% confidence interval for mean change from Day 0 (baseline) to Day 21 in total YMRS score for the difference between test and placebo control treatment will exclude zero for mITT set.	27 days

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Secondary efficacy endpoints	• Percentage of patients with improvement of ≥ 50% in total YMRS from baseline. • Clinical Global Impression-Bipolar (CGI-BP) score at the end of study. • Mean change from baseline to the end of treatment in Montgomery-Åsberge Depression Rating Scale (MADRS) total score. • Improvement in Clinical Global Impression-Severity of Illness scale (CGI-S) score.	21 days

		• Columbia-Suicide Severity Rating Scale (C-SSRS) score at the end of treatment. • Percentage of patients needing lorazepam/diazepam for controlling acute agitation/akathisia. • Percentage of patients requiring rescue medications and withdrawal from the study. • To evaluate trough concentrations of Endoxifen.	

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Jina Pharmaceuticals Inc.

Collaborators

- Novum Pharmaceutical Research Services

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted

2024-09-18

First Submitted that Met QC Criteria

2024-09-19

First Posted

2024-09-23

Study Record Updates

Last Update Submitted that met QC Criteria

2025-03-11

Last Update Posted

2025-03-17

Last Verified

2024-09

More Information

Drug and device information, study documents, and helpful links

Studies a U.S. FDA-Regulated Drug Product

Yes

Studies a U.S. FDA-Regulated Device Product

No

Product Manufactured in and Exported from the U.S.

No

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