A Phase 3 study to assess the safety of KarXT and how it helps in reoccurrence prevention in people with psychosis associated with Alzheimer's Disease as compared to placebo

Estado	**Tipo de Participantes**	**Rangos de Edad**
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase III	162
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	eficacia, farmacocinética	NO

Información

Identificador
2024-511740-11-00 (CTIS)

Cod. Protocolo
KAR-031 (CN012-0026)

Transicionado 2022-001515-10

Área terapéutica
Psiquiatría y Psicología [F] - Desórdenes mentales [F03]|

Enfermedad investigada
Psychosis Associated with Alzheimer's Disease

Título Científico
A Phase 3, Randomized, Double-Blind, Placebo-Controlled Relapse Prevention Study to Evaluate the Safety and Efficacy of KarXT for the Treatment of Psychosis Associated with Alzheimer's Disease (ADEPT-1)

Justificación

No aportado

Objetivo Principal

To evaluate relapse prevention in participants with psychosis associated with AD treated with KarXT compared to placebo

Variables de Evaluación Primaria

Time from randomization to relapse

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

1. To evaluate the time from randomization to first occurrence of treatment discontinuation for any reason or relapse in participants with psychosis associated with AD treated with KarXT compared to placebo.
2. To evaluate the efficacy of KarXT compared with placebo on change from baseline during the Double-blind Randomized Withdrawal Treatment Period, assessed up to relapse, in participants with psychosis associated with AD.
3. To evaluate the safety and tolerability of KarXT compared with placebo in participants with psychosis associated with AD.

Variables de Evaluación Secundaria

Time from randomization to first occurrence of treatment discontinuation for any reason or relapse
Change in NPI-C Core Caregiver Distress score: hallucinations, delusions, agitation, and aggression domains from time of randomization to the end of the Double-blind Randomized Withdrawal Treatment Period or up to relapse, whichever occurs first
To evaluate the safety and tolerability of KarXT Occurrence of AEs, TEAEs, SAEs and TEAEs leading to study withdrawal
AEs including procholinergic (eg, nausea, vomiting, and diarrhea) and anticholinergic symptoms (eg, dry mouth, constipation, urinary retention, blurred vision)
- AESIs such as symptomatic orthostasis, syncope, urinary adverse events, and elevated liver enzymes requiring drug-induced liver injury (DILI) monitoring - Barnes Akathisia Rating Scale (BARS) and Abnormal Involuntary Movement Scale (AIMS) - Body weight and BMI - Orthostatic vital signs
- Clinical laboratory evaluations: hematology, clinical chemistry, coagulation, prolactin levels, urinalysis, and drug screen - 12-lead ECG - Suicidal ideation assessed using the Columbia-Suicide Severity Rating Scale (C-SSRS) - Assessment of cognition as measured by MMSE - IPSS (males only)

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

1. Is a male or female aged 55 to 90 years, inclusive, at Screening (Visit 1).
10. MMSE score of 6 to 24, inclusive, at Screening (Visit 1). For the rest of the inclusion criteria, please refer to the study protocol.
2. Can understand the nature of the study and protocol requirements and provide a signed informed consent (IC) form before any study assessments are performed. If the subject is deemed not competent to provide IC, both the following requirements for consent must be met. a. The subject's legally acceptable representative (LAR) must provide IC. b. The subject must provide informed assent .
3. Meets clinical criteria for the following disorders: a. Possible or probable AD (APPENDIX 1).
4. Has a Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) scan of the brain (completed within the past 5 years) taken during or subsequent to the onset of dementia to rule out other central nervous system (CNS) disease that could account for the ementia syndrome, e.g., major stroke, neoplasm, subdural hematoma. If not available, a non-contrast brain MRI or non-contrast head CT must be done during screening.
5. Living at the same location for a minimum of six weeks before Screening (Visit 1) with the intention of living at the same location throughout the study.
6. Capable of self-locomotion (alone or with the aid of an assistive device) and have an identified caregiver study partner who, in the investigators judgment, has frequent and sufficient contact with the subject (ie, 10 hours per week) on a regular basis to reliably provide accurate information regarding the participants cognitive, behavioral, and functional status, and is willing to: a. Attend all visits and report on subject's status. The caregiver may delegate a responsible substitute, familiar with the subject, to accompany the subject to Visits 3, 4, 6, and/or 8 ONLY as these visits do not include caregiver scales. b. Oversee subject compliance with medication and study procedures. c. Participate in the study assessments and provide IC to participate in the study.
7. History of psychotic symptoms (meeting International Psychogeriatric Association [IPA] criteria [1]) for at least 2 months prior to Screening (Visit 1). (Subjects may or may not have symptoms of agitation).
8. CGI-S scale with a score 4 (moderate) at Screening (Visit 1) and baseline (Visit 2). CGI-S requires the assessor to consider aspects of the psychosis prior to providing a global assessment of severity. These aspects include allucinations and delusions.
9. AD subjects are required to meet at least one of the following criteria at Screening (Visit 1) and baseline (Visit 2): a. Moderate to severe delusions, defined as NPI-C: Delusions domain score of 2 on two of the eight items OR b. Moderate to severe hallucinations, defined as NPI-C: Hallucinations domain score of 2 on two of the seven items.

Criterios de Exclusión

1. Psychotic symptoms that are primarily attributable to a condition other than the AD causing dementia e.g., schizophrenia, schizoaffective disorder, delusional disorder, or mood disorder with psychotic features. 10. Personal or family history of symptoms of long QT syndrome. For the rest of the exclusion criteria, please refer to the study protocol. 2. History of major depressive episode with psychotic features during the 12 months prior to Screening (Visit 1). 3. History of a diagnosis of bipolar disorder, schizophrenia, or schizoaffective disorder. 4. Significant or severe medical conditions including pulmonary, hepatic*, renal, hematologic, (eg, obstructive disorders, including conditions that may decrease GI motility, such as ulcerative colitis, intestinal atony, and myasthenia gravis), endocrine, immunologic, dermatologic, neurologic, cardiovascular (eg, untreated or unstable hypertension, clinically significant tachycardia),**or oncologic disease, or any other condition that, in the opinion of the Investigator, could jeopardize the safety of the subject, ability to complete or comply with the study procedures or validity of the study results. *Participants with any grade of hepatic impairment will be excluded from the study., inclusive of those with alanine aminotransferase (ALT) or aspartate aminotransferase (AST) 2 times of the upper limit of normal (ULN) or total bilirubin > 2 × ULN, or classified as having mild [Child-Pugh Class A], moderate [Child-Pugh Class B], or severe

[Child-Pugh Class C] grades of hepatic impairment. **History of unstable hypertension or tachycardia as evidenced by: a. Blood pressure of 160/100 mmHg at screening. b. Heart rate of 100 bpm at screening (confirmed by repeat measurement at the investigators discretion). 5. Significant or severe renal impairment based on a screening cutoff for estimated glomerular filtration rate (eGFR) of <50 mL/min/1.73 m2. 6. History of ischemic stroke within 12 months prior to Screening (Visit 1) or any evidence of hemorrhagic stroke. 7. History of cerebral amyloid angiopathy (CAA), epilepsy, central nervous system (CNS) neoplasm, unstable thyroid function, or unexplained syncope. 8. Any of the following: a. New York Heart Association (NYHA) Class 2 or greater congestive heart failure b. Grade 2 or greater angina pectoris c. History of sustained ventricular tachycardia d. History of ventricular fibrillation e. History of torsade de pointes f. History of implantable cardiac defibrillator. 9. Myocardial infarction within the 6 months prior to Screening (Visit 1).

Calendario

(Última actualización: 31/08/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
12/12/2022	10/03/2023	17/05/2023	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
No aportado	No aportado	No aportado	No aportado	No aportado

Promotor

Karuna Therapeutics Inc. United States

Route 206Province Line Road

Contact Person

GSM-CT

003223527611

mg-gsm-ct@bms.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

CEIm Provincial de Sevilla

Avenida Doctor Fedriani 3 41009 Sevilla

administracion.eecc.hvm.sspa@juntadeandalucia.es

955043127

Centros

Activo (03/04/2023)

Clinica Montecanal S.L.

Zaragoza

ZARAGOZA

Neurology

Activo (28/03/2023)

COMPLEJO ASISTENCIAL DE ZAMORA

Zamora

ZAMORA

Activo (29/03/2023)

Complejo Asistencial De Zamora Hospital Provincial De Zamora

Zamora

ZAMORA

Psychiatry

Activo (23/05/2023)

Complejo Asistencial Universitario De Salamanca

Salamanca

SALAMANCA

Centro de Salud San Juan - Unidad de Investigación Neurociencias

Cerrado (19/02/2024)

Fundación ACE Instituto Catalán de Neurociencias

Barcelona

BARCELONA

Activo (19/03/2023)

HOSPITAL RECOLETAS SALUD VICTORIA EUGENIA

Sevilla

SEVILLA

Cerrado (18/08/2026)

HOSPITAL UNIVERSITARIO DE LA PRINCESA

Madrid

MADRID

Activo (05/04/2023)

HOSPITAL UNIVERSITARIO RIO HORTEGA

Valladolid

VALLADOLID

Activo (31/03/2023)

HOSPITAL VIAMED MONTECANAL

Zaragoza

ZARAGOZA

Activo (21/03/2023)

Hospital Victoria Eugenia De La Cruz Roja Espanola

Sevilla

SEVILLA

Neurology

Medicamentos

KarXT
CAPSULE
ORAL

-
Principios Activos: N/A

Experimental

KarXT
CAPSULE
ORAL

-
Principios Activos: N/A

Experimental

KarXT
CAPSULE
ORAL

-
Principios Activos: N/A

Experimental

KarXT
CAPSULE
ORAL

-
Principios Activos: N/A

Experimental

KarXT
CAPSULE
ORAL

-
Principios Activos: N/A

Experimental

Sin resultados

A Phase 3 study to assess the safety of KarXT and how it helps in reoccurrence prevention in people with psychosis associated with Alzheimer's Disease as compared to placebo

State	**Type of participants**	**Age Ranges**
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase III	162
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	effectiveness, pharmacokinetics	NO

Information

Identifier
2024-511740-11-00 (CTIS)

Protocol Code
KAR-031 (CN012-0026)

Transitioned 2022-001515-10

Therapeutic area
Psychiatry and Psychology [F] - Mental Disorders [F03]|

Investigated Disease
Psychosis Associated with Alzheimer's Disease

Scientific Title
A Phase 3, Randomized, Double-Blind, Placebo-Controlled Relapse Prevention Study to Evaluate the Safety and Efficacy of KarXT for the Treatment of Psychosis Associated with Alzheimer's Disease (ADEPT-1)

Rationale

Not provided

Main Objective

To evaluate relapse prevention in participants with psychosis associated with AD treated with KarXT compared to placebo

Primary Endpoints

Time from randomization to relapse

Temporary moments of secondary assessment

Not provided

Secondary Objective

1. To evaluate the time from randomization to first occurrence of treatment discontinuation for any reason or relapse in participants with psychosis associated with AD treated with KarXT compared to placebo.
2. To evaluate the efficacy of KarXT compared with placebo on change from baseline during the Double-blind Randomized Withdrawal Treatment Period, assessed up to relapse, in participants with psychosis associated with AD.
3. To evaluate the safety and tolerability of KarXT compared with placebo in participants with psychosis associated with AD.

Secondary Endpoints

Time from randomization to first occurrence of treatment discontinuation for any reason or relapse
Change in NPI-C Core Caregiver Distress score: hallucinations, delusions, agitation, and aggression domains from time of randomization to the end of the Double-blind Randomized Withdrawal Treatment Period or up to relapse, whichever occurs first
To evaluate the safety and tolerability of KarXT Occurrence of AEs, TEAEs, SAEs and TEAEs leading to study withdrawal
AEs including procholinergic (eg, nausea, vomiting, and diarrhea) and anticholinergic symptoms (eg, dry mouth, constipation, urinary retention, blurred vision)
- AESIs such as symptomatic orthostasis, syncope, urinary adverse events, and elevated liver enzymes requiring drug-induced liver injury (DILI) monitoring - Barnes Akathisia Rating Scale (BARS) and Abnormal Involuntary Movement Scale (AIMS) - Body weight and BMI - Orthostatic vital signs
- Clinical laboratory evaluations: hematology, clinical chemistry, coagulation, prolactin levels, urinalysis, and drug screen - 12-lead ECG - Suicidal ideation assessed using the Columbia-Suicide Severity Rating Scale (C-SSRS) - Assessment of cognition as measured by MMSE - IPSS (males only)

Temporary moments of secondary assessment

Not provided

Inclusion criteria

1. Is a male or female aged 55 to 90 years, inclusive, at Screening (Visit 1).
10. MMSE score of 6 to 24, inclusive, at Screening (Visit 1). For the rest of the inclusion criteria, please refer to the study protocol.
2. Can understand the nature of the study and protocol requirements and provide a signed informed consent (IC) form before any study assessments are performed. If the subject is deemed not competent to provide IC, both the following requirements for consent must be met. a. The subject's legally acceptable representative (LAR) must provide IC. b. The subject must provide informed assent .
3. Meets clinical criteria for the following disorders: a. Possible or probable AD (APPENDIX 1).
4. Has a Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) scan of the brain (completed within the past 5 years) taken during or subsequent to the onset of dementia to rule out other central nervous system (CNS) disease that could account for the ementia syndrome, e.g., major stroke, neoplasm, subdural hematoma. If not available, a non-contrast brain MRI or non-contrast head CT must be done during screening.
5. Living at the same location for a minimum of six weeks before Screening (Visit 1) with the intention of living at the same location throughout the study.
6. Capable of self-locomotion (alone or with the aid of an assistive device) and have an identified caregiver study partner who, in the investigators judgment, has frequent and sufficient contact with the subject (ie, 10 hours per week) on a regular basis to reliably provide accurate information regarding the participants cognitive, behavioral, and functional status, and is willing to: a. Attend all visits and report on subject's status. The caregiver may delegate a responsible substitute, familiar with the subject, to accompany the subject to Visits 3, 4, 6, and/or 8 ONLY as these visits do not include caregiver scales. b. Oversee subject compliance with medication and study procedures. c. Participate in the study assessments and provide IC to participate in the study.
7. History of psychotic symptoms (meeting International Psychogeriatric Association [IPA] criteria [1]) for at least 2 months prior to Screening (Visit 1). (Subjects may or may not have symptoms of agitation).
8. CGI-S scale with a score 4 (moderate) at Screening (Visit 1) and baseline (Visit 2). CGI-S requires the assessor to consider aspects of the psychosis prior to providing a global assessment of severity. These aspects include allucinations and delusions.
9. AD subjects are required to meet at least one of the following criteria at Screening (Visit 1) and baseline (Visit 2): a. Moderate to severe delusions, defined as NPI-C: Delusions domain score of 2 on two of the eight items OR b. Moderate to severe hallucinations, defined as NPI-C: Hallucinations domain score of 2 on two of the seven items.

Exclusion criteria

1. Psychotic symptoms that are primarily attributable to a condition other than the AD causing dementia e.g., schizophrenia, schizoaffective disorder, delusional disorder, or mood disorder with psychotic features. 10. Personal or family history of symptoms of long QT syndrome. For the rest of the exclusion criteria, please refer to the study protocol. 2. History of major depressive episode with psychotic features during the 12 months prior to Screening (Visit 1). 3. History of a diagnosis of bipolar disorder, schizophrenia, or schizoaffective disorder. 4. Significant or severe medical conditions including pulmonary, hepatic*, renal, hematologic, (eg, obstructive disorders, including conditions that may decrease GI motility, such as ulcerative colitis, intestinal atony, and myasthenia gravis), endocrine, immunologic, dermatologic, neurologic, cardiovascular (eg, untreated or unstable hypertension, clinically significant tachycardia),**or oncologic disease, or any other condition that, in the opinion of the Investigator, could jeopardize the safety of the subject, ability to complete or comply with the study procedures or validity of the study results. *Participants with any grade of hepatic impairment will be excluded from the study., inclusive of those with alanine aminotransferase (ALT) or aspartate aminotransferase (AST) 2 times of the upper limit of normal (ULN) or total bilirubin > 2 × ULN, or classified as having mild [Child-Pugh Class A], moderate [Child-Pugh Class B], or severe

[Child-Pugh Class C] grades of hepatic impairment. **History of unstable hypertension or tachycardia as evidenced by: a. Blood pressure of 160/100 mmHg at screening. b. Heart rate of 100 bpm at screening (confirmed by repeat measurement at the investigators discretion). 5. Significant or severe renal impairment based on a screening cutoff for estimated glomerular filtration rate (eGFR) of <50 mL/min/1.73 m2. 6. History of ischemic stroke within 12 months prior to Screening (Visit 1) or any evidence of hemorrhagic stroke. 7. History of cerebral amyloid angiopathy (CAA), epilepsy, central nervous system (CNS) neoplasm, unstable thyroid function, or unexplained syncope. 8. Any of the following: a. New York Heart Association (NYHA) Class 2 or greater congestive heart failure b. Grade 2 or greater angina pectoris c. History of sustained ventricular tachycardia d. History of ventricular fibrillation e. History of torsade de pointes f. History of implantable cardiac defibrillator. 9. Myocardial infarction within the 6 months prior to Screening (Visit 1).

Calendar

(Last Update: 31/08/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
12/12/2022	10/03/2023	17/05/2023	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
Not aported	Not aported	Not aported	Not aported	Not aported

Sponsor

Karuna Therapeutics Inc. United States

Route 206Province Line Road

Contact Person

GSM-CT

003223527611

mg-gsm-ct@bms.com

Monetary support: N/A

Sponsor type: Commercial

Ceim

CEIm Provincial de Sevilla

Avenida Doctor Fedriani 3 41009 Sevilla

administracion.eecc.hvm.sspa@juntadeandalucia.es

955043127

Sites

Active (03/04/2023)

Clinica Montecanal S.L.

Zaragoza

ZARAGOZA

Neurology

Active (28/03/2023)

COMPLEJO ASISTENCIAL DE ZAMORA

Zamora

ZAMORA

Active (29/03/2023)

Complejo Asistencial De Zamora Hospital Provincial De Zamora

Zamora

ZAMORA

Psychiatry

Active (23/05/2023)

Complejo Asistencial Universitario De Salamanca

Salamanca

SALAMANCA

Centro de Salud San Juan - Unidad de Investigación Neurociencias

Closed (19/02/2024)

Fundación ACE Instituto Catalán de Neurociencias

Barcelona

BARCELONA

Active (19/03/2023)

HOSPITAL RECOLETAS SALUD VICTORIA EUGENIA

Sevilla

SEVILLA

Closed (18/08/2026)

HOSPITAL UNIVERSITARIO DE LA PRINCESA

Madrid

MADRID

Active (05/04/2023)

HOSPITAL UNIVERSITARIO RIO HORTEGA

Valladolid

VALLADOLID

Active (31/03/2023)

HOSPITAL VIAMED MONTECANAL

Zaragoza

ZARAGOZA

Active (21/03/2023)

Hospital Victoria Eugenia De La Cruz Roja Espanola

Sevilla

SEVILLA

Neurology

Medication

KarXT
CAPSULE
ORAL

-

Active Principles: N/A

Experimental

KarXT
CAPSULE
ORAL

-

Active Principles: N/A

Experimental

KarXT
CAPSULE
ORAL

-

Active Principles: N/A

Experimental

KarXT
CAPSULE
ORAL

-

Active Principles: N/A

Experimental

KarXT
CAPSULE
ORAL

-

Active Principles: N/A

Experimental

No results