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# A Study to evaluate novel KarX and KarT Prototypes versus the KarXT and KarX-EC reference following single doses, and to explore the effect of food after multiple doses of selected prototypes in healthy adult participants

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| **Submission date**<br>25/06/2025 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[ ] Protocol<br>[ ] Statistical analysis plan<br>[ ] Results<br>[ ] Individual participant data<br>[X] Record updated in last year |
| **Registration date**<br>26/06/2025 | **Overall study status**<br>Completed | |
| **Last Edited**<br>26/06/2025 | **Condition category**<br>Mental and Behavioural Disorders | |

## Plain English summary of protocol

Background and study aims
The Sponsor is developing a new test medicine which is a new formulation of a previously tested medicine, KarXT. Currently it is marketed in the USA to treat schizophrenia in adults, but may cause further unwanted side effects in younger patients. The new form of the test medicine is a potential treatment for autism which is a neuropsychiatric condition (mental disorder affecting the nervous system including the brain) and developmental disorder (condition affecting brain development and growth) that affects how people interact with others, communicate, learn and behave.

This 2-part study will compare side effects and blood levels in healthy volunteers after giving different forms of the test medicine compared to a reference test medicine. It may also explore the effect of food on the test medicine.

Who can participate?
Healthy men and women aged 18-55 years.

What does the study involve?
In Parts 1 and 2 volunteers will receive single doses of new forms of the test medicine on up to 2 and 3 occasions respectively, and a reference form of the test medicine on 1 occasion, as capsules by mouth. After this an additional Study Visit may be required in which volunteers will receive either doses of 1 form of the test medicine that they previously received or a new form twice a day for 21 days. Doses may be given with soft food for the last 9 days. They'll stay in the clinic for up to 25 nights on up to 2 (Part 1) and 3 (Part 2) occasions, and take up to 12 (Part 1) and 13 (Part 2) weeks to finish the study.

What are the possible benefits and risks of participating?
Participants get no medical benefit from taking part in the study. However, development of a treatment for younger patients with autism may benefit the population as a whole. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form. Volunteers are closely monitored during the study and safety assessments are performed regularly.

Where is the study run from?
Bristol-Myers Squibb Services Unlimited Company (Ireland)

When is the study starting and how long is it expected to run for?
April 2025 until February 2026

Who is funding the study?
Bristol-Myers Squibb Services Unlimited Company (Ireland)

Who is the main contact?
BMS Clinical Trials Contact Center, Clinical.Trials@bms.com

# Contact information

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Public, Scientific

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# Additional identifiers

### Clinical Trials Information System (CTIS)
Nil known

### Integrated Research Application System (IRAS)
1011809

### Protocol serial number
Study Code: CN0120043, Quotient Code: QSC303233

# Study information

### Scientific Title
A Phase 1, 2-part, open-label study to evaluate the pharmacokinetics of novel KarX (BMS-986519) and KarT (BMS-986520) Prototypes versus the KarXT (BMS-986510) and KarX-EC (BMS-986519) Reference following single doses, and to explore the effect of food after multiple doses of selected prototypes in healthy adult participants

### Study objectives
Primary objectives:
1. To determine the primary plasma PK parameters of xanomeline and trospium when administered as KarX + KarT + KarX-EC/MR prototypes (2 prototypes in Part 1 and up to 4 prototypes in Part 2) as single doses relative to the KarXT + KarX-EC reference formulation
2. To determine the plasma PK parameters of xanomeline and trospium when administered as KarX + KarT + KarX-EC Prototype X (selected prototype in Part 1)/KarX + KarT + KarX-MR Prototype X (selected prototype in Part 2) at steady state in a fasted state and when administered with a soft food or liquid vehicle

Secondary objectives:
1.To assess the safety and tolerability of xanomeline and trospium when administered as KarX + KarT + KarX-EC/MR prototypes and KarXT + KarX-EC reference
2. To compare the relative bioavailability of xanomeline and trospium when administered as KarX + KarT + KarX-EC prototypes (Part 1)/KarX + KarT + KarX-MR prototypes (Part 2) as single doses in a fasted state vs when administered as KarXT + KarX-EC reference as a single dose in the fasted state
3. To compare the relative bioavailability of xanomeline and trospium when administered as KarX + KarT + KarX-EC Prototype X (selected prototype in Part 1)/KarX + KarT + KarX-MR Prototype X (selected prototype in Part 2) in a fasted state vs when administered with a soft food or liquid vehicle (eg, yoghurt, applesauce or a liquid to drink)

### Ethics approval required
Ethics approval required

### Ethics approval(s)
approved 11/06/2025, North East - York Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8241; york.rec@hra.nhs.uk), ref: 25/NE/0059

### Study design
Single-center 2-part open-label randomized single- and multiple-dose study

## Primary study design
Interventional

## Study type(s)
Safety

## Health condition(s) or problem(s) studied
Autism spectrum disorder. Study to be conducted in healthy volunteers.

## Interventions
In Part 1, it is planned that each participant will receive a single oral dose of KarXT + KarX-EC reference on a single occasion and single oral doses of KarX + KarT + KarX-EC prototypes on 2 occasions in the fasted state in Periods 1 to 3, with a minimum washout of 3 days between dosing in each period. In optional Period 4, participants may also receive oral doses of a selected KarX + KarT + KarX-EC prototype on 21 consecutive days BID in the fasted state (doses on Days 13 to 21 will be administered with a soft food or liquid vehicle). Including a 28-day screening period and a follow-up phone call 28 days (+ 2 days) post final dose of study intervention, the total study duration for Part 1 is planned to be approximately 12 weeks if Period 4 is executed, and approximately 10 weeks if Period 4 is not executed.

In Part 2, it is planned that each participant will receive a single oral dose of KarXT + KarX-EC reference on a single occasion and single oral doses of KarX + KarT + KarX-MR prototypes on up to 3 separate occasions in the fasted state in Periods 1 to 3 and optional Period 4, with a minimum washout of 3 days between dosing in each period. In optional Period 5, participants may also receive multiple oral doses of a selected KarX + KarT + KarX-MR prototype, or a new KarX + KarT + KarX-MR prototype not previously administered, on 21 consecutive days BID in the fasted state (doses on Days 13 to 21 will be administered with a soft food or liquid vehicle). Including a 28-day screening period and a follow-up phone call 28 days (+ 2 days) post final dose of study intervention, the total study duration for Part 2 is planned to be: approximately 13 weeks if Periods 4 and 5 are executed; approximately 12 weeks if Period 4 is not executed and Period 5 is executed; and approximately 10 weeks if Periods 4 and 5 are not executed.

## Intervention Type
Drug

## Phase
Phase I

## Drug/device/biological/vaccine name(s)
Xanomeline/Trospium Chloride Capsule, Xanomeline Enteric Capsule, Xanomeline IR minitablets in Capsule, Trospium Chloride IR minitablets in capsule, Xanomeline EC1 minitablets in capsule, Xanomeline EC2 minitablets in capsule

## Primary outcome(s)
1. Maximum observed concentration (Cmax) is measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints up to Day 23
2. Time of maximum observed concentration (Tmax) is measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints up to Day 23
3. Area under the concentration-time curve from time zero to time of last quantifiable concentration (AUC(0-T)) is measured using plasma drug concentration assay at pre-dose and at

multiple post-dose timepoints up to Day 23
4. Area under the concentration-time curve from time zero extrapolated to infinite time (AUC (INF)) is measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints up to Day 23
5. Area under the concentration-time curve in one dosing interval (AUC(TAU)) is measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints within each dosing interval up to Day 23
6. Concentration at the end of a dosing interval (Ctau) is measured using plasma drug concentration assay at the end of each dosing interval up to Day 23
7. Apparent total body clearance (CLT/F) is measured using plasma drug concentration assay and non-compartmental analysis at pre-dose and at multiple post-dose timepoints up to Day 23
8. Effective elimination half-life during dosing interval (T-HALF(eff)) is measured using plasma drug concentration assay and non-compartmental analysis at pre-dose and at multiple post-dose timepoints up to Day 23

## Key secondary outcome(s))

1. Number of participants with treatment-emergent adverse events (TEAEs) is measured using adverse event case report forms at screening, throughout treatment, and up to 30 days after final dose of study intervention
2. Number of participants with serious adverse events (SAEs) is measured using adverse event case report forms at screening, throughout treatment, and up to 30 days after final dose of study intervention
3. Number of participants with adverse events of special interest (AESIs) is measured using adverse event case report forms at screening, throughout treatment, and up to 30 days after final dose of study intervention
4. Number of participants with adverse events leading to discontinuation is measured using adverse event case report forms at screening, throughout treatment, and up to 30 days after final dose of study intervention
5. Number of participants with vital signs abnormalities is measured using vital signs assessments (blood pressure, heart rate, respiratory rate, temperature) at screening, baseline, during treatment visits, and up to 30 days after final dose of study intervention
6. Number of participants with electrocardiogram (ECG) abnormalities is measured using 12-lead ECG at screening, baseline, during treatment visits, and up to 30 days after final dose of study intervention
7. Number of participants with physical examination abnormalities is measured using structured physical examination at screening, baseline, during treatment visits, and up to 30 days after final dose of study intervention
8. Number of participants with clinical laboratory abnormalities is measured using clinical laboratory tests (hematology, biochemistry, urinalysis) at screening, baseline, during treatment visits, and up to 30 days after final dose of study intervention
9. Number of participants with Columbia-Suicide Severity Rating Scale (C-SSRS) abnormalities is measured using the Columbia-Suicide Severity Rating Scale at screening, baseline, during treatment visits, and up to 30 days after final dose of study intervention
10. Geometric mean ratio of Cmax is measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints up to Day 23
11. Geometric mean ratio of AUC(0-T) is measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints up to Day 23
12. Geometric mean ratio of AUC(INF) is measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints up to Day 23
13. Geometric mean ratio of AUC(TAU) is measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints up to Day 23

### Completion date
28/02/2026

## Eligibility

### Key inclusion criteria
1. Participants must have signed and dated a REC-approved written ICF in accordance with regulatory, local, and institutional guidelines. This ICF must be obtained before performing any protocol-related procedures.
2. Participant must be willing and able to complete all study-specific procedures and visits.
3. Healthy males and healthy females (IOCBP or INOCBP). The definition of healthy will be according to the assessment of the investigator, as based on a complete medical history including a physical examination, vital signs, orthostatic vital signs, single 12-lead ECG, C SSRS, and clinical laboratory tests without any clinically significant abnormalities at screening and Period 1 admission.
4. Body mass index of 18.0 kg/m² to 32.0 kg/m², inclusive, at screening.
5. Participant must be 18 to 55 years of age, inclusive, at the time of signing the ICF.
6. Female (as assigned at birth) participants must agree to follow instructions for method(s) of contraception as described in the Clinical Protocol.
7. A male (as assigned at birth) who is sexually active with IOCBP must agree to follow instructions for method(s) of contraception as described in the Clinical Protocol.

### Participant type(s)
Healthy volunteer

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 years

### Upper age limit
55 years

### Sex
All

### Key exclusion criteria
1. History or presence of clinically significant cardiovascular, pulmonary, hepatic, renal, hematologic, GI (eg, obstructive disorders [including conditions that may decrease GI motility, such as ulcerative colitis, intestinal atony, and myasthenia gravis]), endocrine, immunologic, dermatologic, psychiatric, neurologic, or oncologic disease or any other condition that, in the opinion of the investigator, would jeopardize the safety of the participant or the validity of the study results.
Note: participants who have had basal cell cancer successfully excised at least 6 months prior to screening are permitted.
2. Participants with cirrhosis, biliary duct abnormalities, hepatobiliary carcinoma, and/or active

hepatic viral infections based on LFT results.
3. Any significant acute or chronic medical illness (in the assessment of the investigator).
4. History or high risk of urinary retention, gastric retention, or narrow angle glaucoma or known history of prostate hypertrophy or nocturia.
5. Current or recent (within 3 months of study intervention administration) GI disease that could possibly affect drug absorption, distribution, metabolism, and excretion (eg, bariatric procedure).
6. Any major surgery, including GI surgery (eg, cholecystectomy and any other GI surgery) that could impact upon the absorption of study intervention (uncomplicated appendectomy and hernia repair are acceptable).
7. History of irritable bowel syndrome (with or without constipation) or serious constipation requiring treatment within the last 6 months prior to screening.
8. Risk for suicidal behavior at screening as determined by the investigator's clinical assessment and the C-SSRS scoring with an answer "Yes" to item 4 or 5 within 6 months of screening, or suicide attempt within 12 months of screening.
Note: If the participant is excluded based on C-SSRS responses, the investigator must refer the participant to emergency care or mental health evaluation and intervention as appropriate per local standard of care.
9. History of ischemic or hemorrhagic stroke within 12 months prior to screening.
10. Presence of any factors that would predispose the participant to develop infection (eg, rectal fissures, poor dentition, open skin lesions).
11. Any serious acute or chronic bacterial or viral infection (eg, pneumonia, septicemia) within 3 months prior to screening.
12. History or any evidence of active infection or febrile illness within 7 days prior to first dose of study intervention (eg, bronchopulmonary, urinary, or GI).
13. History of cerebral amyloid angiopathy, epilepsy, CNS neoplasm, unstable thyroid function, or unexplained syncope.
14. History of unstable hypertension or tachycardia as evidenced by:
14.1. Blood pressure of ≥ 160/100 mmHg at screening.
14.2. Heart rate of ≥ 110 bpm at screening.
15. Any of the following currently or historically:
15.1. New York Heart Association Class II or greater congestive heart failure (Class II - slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, shortness of breath or chest pain).
15.2. Grade 2 or greater angina pectoris (Grade 2 - slight limitation of ordinary activities when they are performed rapidly, after meals, in cold, in wind, under emotional stress, during the first few hours after waking up, but also walking uphill, climbing more than one flight of ordinary stairs at a normal pace and in normal conditions).
15.3. Sustained ventricular tachycardia.
15.4. Ventricular fibrillation.
15.5. Torsade de pointes.
15.6. Implantable cardiac defibrillator.
15.7. Brugada syndrome.
16. Myocardial infarction within the 6 months prior to screening.
17. Personal or family history of symptoms of long QT syndrome as evaluated by the investigator.
18. History of chronic psychiatric disorders, depression or anxiety within the past 6 months.
19. Individuals who are pregnant, breastfeeding, or less than 3 months postpartum.
20. Inability to comply with restrictions and prohibited treatments as listed in the Clinical Protocol.
21. Prior exposure to KarXT in the 28 days or 5 T-HALFs prior to first dose of study intervention, whichever is longer.
22. Exposure to any experimental or investigational drug agent (including placebo) within 90

days or 5 T HALFs (if known), whichever is longer, prior to study intervention administration.
23. History of incompletely treated mycobacterium TB infection, as indicated by:
23.1. Participant's medical records documenting incomplete treatment for mycobacterium TB.
23.2. Participant's self-reported history of incomplete treatment for mycobacterium TB.
Note: Participants with a history of TB who have undergone treatment accepted by the local health authorities (documented) may be eligible for study entry.
24. Evidence of organ dysfunction or any clinically significant deviation from normal in physical examination, vital signs, single 12-lead ECG, or clinical laboratory determinations beyond what is consistent with the target population reference ranges at screening or pre first dose of study intervention.
25. Any of the following on single 12-lead ECG prior to study intervention administration, confirmed by repeat:
25.1. PR ≥ 210 msec.
25.2. QRS ≥ 120 msec.
25.3. QT ≥ 500 msec.
25.4.QTcF ≥ 450 msec.
26. Participant has a supine blood pressure measurement that is out of range (systolic blood pressure: 100 to 140 mmHg; diastolic blood pressure 50 to 90 mmHg) at screening or pre first dose of study intervention. Repeats may be measured at investigator discretion.
27. Participants with supine heart rate out of range (50 to 90 bpm) at screening or pre first dose of study intervention. Repeats may be measured at investigator discretion.
28. Positive urine screen for drugs of abuse at screening or Period 1 Day -1.
29. Positive alcohol breath test on at screening or Period 1 Day -1.
30. Positive blood screen for HCV antibody, HBsAg or HIV-1 and HIV-2 antibody at screening.
31. Coagulation with INR > 1.5 at screening.
32. Confirmed platelet count < 100× 103 µL at screening.
33. AST or ALT > 1.5× ULN at screening.
34. Bilirubin > 1.5× ULN. Participants with Gilbert's syndrome are allowed (maximum total bilirubin not more than 2× ULN, with direct bilirubin being no more than 35% of total bilirubin).
35. Serum creatinine or blood urea nitrogen > ULN or absolute eGFR of < 90 mL/min calculated by the CKD-EPI equation at screening.
36. Creatine (phospho)kinase > 1000 U/L at screening.
37. Sodium < the lower limit of normal at screening.
38. History of allergy/hypersensitivity to any component (including excipients) of the study intervention or related compounds.
39. History of any significant drug allergy (such as anaphylaxis or hepatotoxicity).
40. Prisoners or participants who are involuntarily incarcerated. (Note: Under certain specific circumstances and only in countries where local regulations permit, a person who has been imprisoned while on study may be permitted to continue as a participant. Strict conditions apply, and Sponsor approval is required).
41. Current involuntary hospitalization.
42. Participants who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness.
43. Inability to tolerate oral medication, to be venipunctured/cannulated (due to unsuitable veins) and/or tolerate venous access.
44. Regular alcohol consumption in males > 21 units per week and in females > 14 units per week (1 unit = ½ pint beer, or a 25 mL shot of 40% spirit, 1.5 to 2 units = 125 mL glass of wine, depending on type).
45. History (within 1 year of first dose) of drug or alcohol use disorder as defined in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Diagnostic Criteria for Drug and Alcohol Abuse.
46. Prior participation in this study ie, participants in Part 1 are not permitted to take part in Part

2.
47. Participant is an employee of the investigator, study site, Sponsor or Contract Research Organization, with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator.
48. Donation of blood to a blood bank or in a clinical study (except a screening visit) within 4 weeks prior to first dose of study intervention (within 2 weeks for plasma only).
49. Blood transfusion within 4 weeks prior to first dose of study intervention.

### Date of first enrolment
27/06/2025

### Date of final enrolment
28/02/2026

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre
**Quotient Sciences Limited**
Mere Way, Ruddington Fields, Ruddington
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## Sponsor information

### Organisation
Bristol-Myers Squibb Services Unlimited Company

## Funder(s)

### Funder type
Industry

### Funder Name
Bristol-Myers Squibb Services Unlimited Company

# Results and Publications

### Individual participant data (IPD) sharing plan

BMS will provide access to individual anonymized participant data upon request from qualified researchers, and subject to certain criteria.
Additional information regarding Bristol Myers Squibb's data sharing policy and process can be found at:
https://www.bms.com/researchers-and-partners/clinical-trials-and-research/disclosurecommitment.html

### IPD sharing plan summary

Stored in non-publicly available repository