# A drug-drug interaction study of DNL343 on midazolam in healthy participants

Submission date	Recruitment status No longer recruiting	<ul><li>Prospectively registered</li></ul>		
12/04/2023		☐ Protocol		
Registration date	Overall study status Completed	Statistical analysis plan		
21/04/2023		[X] Results		
Last Edited	Condition category	[] Individual participant data		
07/06/2024	Other			

### Plain English summary of protocol

Background and Study Aims

This is a drug-drug interaction (DDI) study to investigate the effect of DNL343 on the pharmacokinetics (PK) of oral midazolam (MDZ). A DDI study is conducted to see how the two drugs interact in the body; evaluating PK is figuring out how participants' bodies handle a drug or drugs in combination.

Who Can Participate?

Healthy volunteers aged 18 to 65 years.

What does the Study Involve?

The total duration of each participant's involvement in the study will be approximately 53 days from screening through follow-up.

What are the Possible Benefits and Risks of Participating?

Healthy volunteers will not receive any health benefit (beyond that of an assessment of their medical status) from participating in the study. The risks of participation are primarily those associated with adverse reactions to the study interventions and procedures. DNL343 has been extensively evaluated in nonclinical studies (ie, animal studies and studies done with cells in a petri dish) and evaluation in clinical studies to characterize its safety profile.

Where is the study run from? Denali Therapeutics Inc. (USA)

When is the study starting and how long is it expected to run for? November 2022 to June 2023

Who is funding the study?
Denali Therapeutics Inc. (USA)

Who is the main contact?

Clinical Trials Disclosures Group at Denali Therapeutics, clinical-trials-disclosures@dnli.com

# Contact information

# Type(s)

Principal investigator

#### Contact name

Dr Helen Philpott

### Contact details

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### Type(s)

Public, Scientific

#### Contact name

Ms Gabrielle Brill

### Contact details

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# Type(s)

**Public** 

#### Contact name

Dr Clinical Trials Disclosures Group -

#### Contact details

Denali Therapeutics

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United States of America

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None provided clinical-trials-disclosures@dnli.com

# Additional identifiers

### Clinical Trials Information System (CTIS)

2022-003926-38

## Integrated Research Application System (IRAS)

1007175

# ClinicalTrials.gov (NCT)

Nil known

### Protocol serial number

IRAS 1007175

# Study information

### Scientific Title

A drug-drug interaction study of the effect of DNL343 on midazolam pharmacokinetics in healthy participants

### **Study objectives**

To assess the pharmacokinetics (PK) of midazolam (MDZ) in the presence and absence of DNL343

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

- 1. Approved 10/03/2023, Wales Research Ethics Committee 2 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)2922941119; Wales. REC2@wales.nhs.uk), ref: 23/WA/0041
- 2. Approved 14/03/2023, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 50398/0011/001-0001

The HRA approved the deferral of the publication of trial details. Full details were added after the deferral ended.

## Study design

Fixed sequence crossover drug-drug interaction study

# Primary study design

Interventional

# Study type(s)

Other

# Health condition(s) or problem(s) studied

Healthy volunteers

#### **Interventions**

Treatment Period 1: Single oral dose of MDZ

Treatment Period 2: Once daily oral dose of DNL343 for 14 days then coadministered with a single dose of MDZ on the 14th day

### Intervention Type

Drug

### **Phase**

Phase I

### Drug/device/biological/vaccine name(s)

DNL343, midazolam (MDZ)

### Primary outcome(s)

MDZ PK parameters, as measured by laboratory analysis of plasma concentrations from blood samples including, but not limited to, the following at multiple timepoints over 25 days:

- 1. Maximum concentration (Cmax)
- 2. Time to reach maximum concentration (tmax)
- 3. Area under the concentration-time curve from time zero to infinity (AUC∞)
- 4. Terminal elimination half-life (t1/2)

### Key secondary outcome(s))

- 1. Incidence of treatment-emergent adverse events (TEAEs) and SAEs as reported by the participant continuously over 25 days:
- 2. MDZ metabolite PK parameters, as measured by laboratory analysis of plasma concentrations from blood samples including, but not limited to, the following at multiple timepoints over 25 days:
- 2.1 Maximum concentration (Cmax)
- 2.2 Time to reach maximum concentration (tmax)
- 2.3 Area under the concentration-time curve from time zero to infinity (AUC∞)
- 2.4 Terminal elimination half-life (t1/2)
- 3. DNL343 PK parameters, as measured by laboratory analysis of plasma concentrations from blood samples including, but not limited to, the following at multiple timepoints over 25 days:
- 3.1 AUC during a dosage interval (tau) (AUCt)
- 3.2 Maximum concentration at steady state (Cmax,ss)

### Completion date

09/06/2023

# **Eligibility**

### Key inclusion criteria

- 1. Healthy female participants of non-childbearing potential or healthy male participants between 18 and 65 years of age, inclusive
- 2. Body mass index (BMI) between 18.5 and 30  $kg/m^2$  and a body weight of at least 50 kg

# Participant type(s)

Healthy volunteer

# Healthy volunteers allowed

No

### Age group

Adult

### Lower age limit

18 years

### Upper age limit

65 years

### Sex

All

### Total final enrolment

16

### Key exclusion criteria

- 1. Any history of hepatic, pulmonary, and/or renal disease
- 2. History of serious adverse reaction or serious hypersensitivity to any drug
- 3. History of allergy to any component of the study intervention
- 4. Have any surgical or medical condition affecting drug absorption (eg, gastrectomy)

### Date of first enrolment

29/03/2023

### Date of final enrolment

15/05/2023

# Locations

### Countries of recruitment

United Kingdom

Wales

# Study participating centre

Simbec-Orion Clinical Pharmacology (AKA Simbec Research Ltd)

Merthyr Tydfil Industrial Park Cardiff Road Merthyr Tydfil United Kingdom CF48 4DR

# Sponsor information

### Organisation

Denali Therapeutics Inc.

# Funder(s)

## Funder type

Industry

#### Funder Name

**Denali Therapeutics** 

### Alternative Name(s)

DENALI, Denali Therapeutics Inc.

### **Funding Body Type**

Government organisation

## **Funding Body Subtype**

For-profit companies (industry)

#### Location

United States of America

# **Results and Publications**

## Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study are not expected to be made available because of their high commercial sensitivity and the negligible benefit to the public of publication of results of non-therapeutic clinical trials.

## IPD sharing plan summary

Not expected to be made available

# **Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		25/03/2024	09/05/2024	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes