# nature portfolio

- Accession codes, unique identifiers, or web links for publicly available datasets

- For clinical datasets or third party data, please ensure that the statement adheres to our policy

- A description of any restrictions on data availability

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Last updated by author(s):	16 July 2024

## **Reporting Summary**

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study. For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

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5	ta:	t١	c†	ics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.
n/a Confirmed
The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
X A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
The statistical test(s) used AND whether they are one- or two-sided  Only common tests should be described solely by name; describe more complex techniques in the Methods section.
X A description of all covariates tested
A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i> ) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted Give P values as exact values whenever suitable.
For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i> ), indicating how they were calculated
Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.
Software and code
Policy information about <u>availability of computer code</u>
Data collection
Data analysis WinNonLin, GraphPad Prism v9, ADAPT5
For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.
Data
Policy information about <u>availability of data</u>
All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

The raw data supporting killing kinetics, pharmacokinetics (pre-clinical and clinical), efficacy in animal models are provided as an excel file, "Source data.xlsx"

Research inv	olving hur	man participants, their data, or biological material
Policy information a and sexual orientati		rith <u>human participants or human data</u> . See also policy information about <u>sex, gender (identity/presentation),</u> <u>chnicity and racism</u> .
Reporting on sex	and gender	No exclusion based on sex and gender; Included in reporting
Reporting on race other socially relegroupings		No exclusion based on race, ethnicity or other socially relevant groupings
Population charac	cteristics	Age 18-55
Recruitment		healthy volunteers
Ethics oversight		Bellberry Ethics Committee Australia
Note that full informa	tion on the appro	oval of the study protocol must also be provided in the manuscript.
e		
<u>Field-spe</u>	cific re	porting
Please select the or	ne below that is	the best fit for your research. If you are not sure, read the appropriate sections before making your selection.
X Life sciences	Ве	ehavioural & social sciences
or a reference copy of the	he document with a	all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>
Life scien	ices stu	ıdy design
All studies must disc	close on these p	points even when the disclosure is negative.
Sample size	40 healthy h	uman volunteers
Data exclusions	None	
Replication	6+2 design p	er dose arm (6 on active, 2 on placebo)
Randomization	Randomized	
Blinding	Doube-blind	
Behaviou	ıral & s	ocial sciences study design
All studies must disc	close on these ¡	points even when the disclosure is negative.
Study description		
Research sample		
Sampling strategy	,	

Data collection

Data exclusions

Non-participation

Randomization

Timing

all studies must disclose on	these points even when the disclosure is negative.
Study description	
Research sample	
Sampling strategy	
Data collection	
Timing and spatial scale	
Data exclusions	
Reproducibility	
Randomization	
Blinding	
Field work, collect	tion and transport
Field conditions	
Field conditions  Location	
Location	
Location  Access & import/export  Disturbance  Reporting fo  Ve require information from a system or method listed is relevant.  Materials & experimental involved in the study  Antibodies	r specific materials, systems and methods  uthors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material vant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response     Methods
Location  Access & import/export  Disturbance  Reporting fo  Ve require information from a system or method listed is relevant.  Materials & experimental involved in the study  Materials & Eukaryotic cell lines	r specific materials, systems and methods  uthors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each materivant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response   ntal systems  Methods  n/a   Involved in the study
Location  Access & import/export  Disturbance  Reporting fo  Ve require information from a ystem or method listed is relevant to the study of the st	r specific materials, systems and methods  uthors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material vant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response   ntal systems    Methods
Location  Access & import/export  Disturbance  Reporting fo  We require information from a system or method listed is releved in the study  Materials & experiments  Involved in the study  Antibodies  Location  Authorities  Authorities  Location  Authorities  Authorities  Authorities  Location  Authorities  Aut	r specific materials, systems and methods  uthors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material vant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response   ntal systems    Methods

### Antibodies

Antibodies used
Validation

Eukaryotic cell line	es	
Policy information about <u>ce</u>	Il lines and Sex and Gender in Research	
Cell line source(s)	Cardiac panel CHO cells at Labcorp, UK., HEK293 cell based assays done at Eurofins	
Authentication	Cardiac panel authentication done at Labcorp, UK., HEK293 cell based assay authentication done at Eurofins	
Mycoplasma contamination		
Commonly misidentified I (See <u>ICLAC</u> register)	ines	
Palaeontology and	d Archaeology	
Specimen provenance		
Specimen deposition		
Dating methods		
Tick this box to confirm	n that the raw and calibrated dates are available in the paper or in Supplementary Information.	
Ethics oversight		
Note that full information on th	ne approval of the study protocol must also be provided in the manuscript.	
Animals and other	r research organisms	
Policy information about stu Research	udies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in	
Laboratory animals	MICE, RATS, GUINEA PIGS, DOGS	
Wild animals	NONE	
Reporting on sex	MALES AND FEMALES	
Field-collected samples	NONE	
Ethics oversight	INSTITUTIONAL ANIMAL ETHICS COMMITTEE APPROVAL	
Note that full information on th	ne approval of the study protocol must also be provided in the manuscript.	
Clinical data		
Policy information about <u>cli</u> All manuscripts should comply	nical studies with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.	
Clinical trial registration	ClinicalTrials.gov Identifier: NCT05088421	
Study protocol	PDF enclosed	
Data collection	Plasma and Urine for Pharmcokinetics; ECG and Holter data; Clinical Biochemistry (plasma, renal and liver)	
Outcomes	Primary outcome: safety. Secondary outcome: Pharmacokinetics	

#### Dual use research of concern

Policy information about <u>dual use research of concern</u>

#### Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No Yes	
X Public health	
X National security	
Crops and/or livesto	ock
X Ecosystems	
X Any other significan	nt area
Experiments of concert	n
Does the work involve any	y of these experiments of concern:
No Yes	
X Demonstrate how t	to render a vaccine ineffective
X Confer resistance to	o therapeutically useful antibiotics or antiviral agents
Enhance the viruler	nce of a pathogen or render a nonpathogen virulent
X     Increase transmissil	
X Alter the host range	
	liagnostic/detection modalities
_ _	ization of a biological agent or toxin
Any other potential	lly harmful combination of experiments and agents
Plants	
Seed stocks	
Novel plant genotypes	
Authentication	
Authentication	
ChIP-seq	
Data deposition	
Confirm that both raw	and final processed data have been deposited in a public database such as GEO.
Confirm that you have	e deposited or provided access to graph files (e.g. BED files) for the called peaks.
Data access links May remain private before public	ration.
Files in database submissi	on
Genome browser session (e.g. <u>UCSC</u> )	
Methodology	
Replicates	
Sequencing depth	
Antibodies	
Peak calling parameters	
Data quality	

Flow Cytometry	
Plots Confirm that: The axis labels state the market The axis scales are clearly visib All plots are contour plots with	
	of cells or percentage (with statistics) is provided.
Methodology Sample preparation	
Instrument	
Software	
Cell population abundance	
Gating strategy	
	figure exemplifying the gating strategy is provided in the Supplementary Information.
	o
Magnetic resonance im	aging
Experimental design	
Design type	
Design specifications	
Behavioral performance measures	
Imaging type(s)	
Field strength	
Sequence & imaging parameters	
Area of acquisition	
Diffusion MRI Used	☐ Not used
Preprocessing	
Preprocessing software	
Normalization	
Normalization template	
Noise and artifact removal	
Volume censoring	
Statistical modeling & inferer	ce
Model type and settings	
Effect(s) tested	

Software

nature portfolio
reporting summary

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Specify type of analysis: Whole brain ROI-based Both
Statistic type for inference
(See Eklund et al. 2016)
Correction
Models & analysis
n/a Involved in the study  Functional and/or effective connectivity  Graph analysis  Multivariate modeling or predictive analysis
Functional and/or effective connectivity
Graph analysis
Multivariate modeling and predictive analysis