

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 [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Statistics

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 |
| ☐ | ☒ 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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☒ | ☐ 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. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ 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 d , Pearson's r), indicating how they were calculated |

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection Taimei eCollect v6 EDC.

Data analysis SAS v.9.4, R v.4.4.3 and Phoenix WinNonlin Version 8.3.1 (Certara, Princeton, NJ, USA).

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 [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

Owing to intellectual property, confidentiality obligations and regulations, individual deidentified participant data that underlie the results reported in this article may be available after completion of the first-in human trial with the clinical study report finalization. The request can be sent to the corresponding author (shunlu@sjtu.edu.cn) and the leading clinical site and sponsor will review the request to ensure compliance with intellectual property, confidentiality obligations and regulations and will respond within two weeks. Data are only available upon request to protect the privacy of the company and clinical trial participants. A

signed data access agreement with the sponsor is required before any data can be shared. The trial protocol and statistical analysis plan are available alongside the published article. The molecular structure of GFH375 has been published (referring to the patent number: WO2024061370, Supplementary Fig. 1).

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	Sex is reported in Table 1 of demographics and baseline characteristics of all patients. Sex was determined based on self report by the patient.
Reporting on race, ethnicity, or other socially relevant groupings	All patients enrolled in this study were of East Asian descent. Race and other socially relevant groupings were not included in the analysis of the study.
Population characteristics	Population characteristics are reported in Table 1 of all patients.
Recruitment	Patients with solid tumors were recruited from participating clinics from 15 sites in China. These sites were selected based on factors such as availability of patients within the patient population of this study and investigator expertise. Patients were recruited, screened, and enrolled at the discretion of investigator. All patients had local documented testing results at screening that were used to determine eligibility. Attempts to limit bias were made through study design and site selection to obtain a representative population of patients with solid tumors; however, a limitation is the small size of the study.
Ethics oversight	The protocol was approved by investigator sites and ethics committees from Ethics Committee of Shanghai Chest Hospital; Medical Ethics Committee of Zhejiang Cancer Hospital; Medical Ethics Committee of Hunan Cancer Hospital; Ethics Committee of National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College; Medical Ethics Committee of Sun Yat-sen Memorial Hospital, Sun Yat-sen University; The Ethics Committee of Scientific Research and Clinical Trial, The First Affiliated Hospital of Zhengzhou University; Medical Ethics Committee of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology; Ethics Committee of Shandong Cancer Hospital, Shandong First Medical University; Ethics Committee of The First Affiliated Hospital of Nanjing Medical University; Ethics Committee of Harbin Medical University Cancer Hospital; Ethics committee of The Sixth Affiliated hospital, Sun Yat-sen University; Human Research Ethics Committee of The Second Affiliated Hospital, Zhejiang University School of Medicine; Clinical Research Sub-Committee of the Medical Ethics Committee of The First Affiliated Hospital of China Medical University; Drug Clinical Trial Ethics Committee of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences; Clinical Research Ethics Committee of The First Affiliated Hospital of Anhui Medical University. All patients provided written informed consent before participating in the trial.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	The sample size of this study was determined by practical considerations common in early oncology trials rather than a formal statistical hypothesis.
Data exclusions	All treated patients (those who received at least 1 dose of GFH375) were included in the safety assessment. Efficacy was evaluated in patients who received at least 1 dose of GFH375. Pharmacokinetics were assessed in all patients who received at least 1 dose of GFH375 and provided at least one blood sample with evaluable pharmacokinetic data.
Replication	There is no replication. Assessments were performed on individual patients samples.
Randomization	This was a nonrandomized phase 1/2 study in which patients were assigned directly to GFH375 treatment.
Blinding	This was an open-label, single arm study.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply 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, NCT06500676.
Study protocol	Prototol is available alongside the published article.
Data collection	Patients were enrolled from clinics from 15 sites in China from 09-July-2024 to 09-April-2025. Data were collected through 12-December-2025 for safety data and 13-January-2026 for efficacy data.
Outcomes	Primary and secondary outcomes were pre-defined in the protocol accordingly to the standard safety and tolerability outcomes for an oncology clinical trial, standard pharmacokinetic endpoints, and tumor response criteria (Response Evaluation Criteria in Solid Tumors v1.1). Safety and tolerability were assessed by AEs and clinically significant changes in vital signs, physical exams, electrocardiograms and clinical laboratory tests. Pharmacokinetic parameters were determined using standard noncompartmental methods. Tumor assessments were performed by computed tomography or MRI. The results presented in this article are derived from the phase 1 trial.

Plants

Seed stocks	<i>Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.</i>
Novel plant genotypes	<i>Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.</i>
Authentication	<i>Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.</i>