

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 (<i>n</i>) 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> 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 <i>d</i> , Pearson's <i>r</i>), 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	Medidata RAVE 2018.2.4
Data analysis	FlowJo TM V10 GraphPad Prism v9.4

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](#)

Requests must be made to datarequest@elicio.com, with responses provided within 30 days of request. To ensure that data sharing is consistent with the underlying study consent, de-identified patient data that can be shared will be done under data transfer agreements. Investigators and institutions who agree to the

terms of the data transfer agreement, which will include, but will not be limited to, terms to address the use of these data for the purposes of a specific project and for research purposes only, to prohibit attempts to re-identify the data and to protect the confidentiality of the data, will be granted access to the data. Elicio Therapeutics will then facilitate the transfer of the requested de-identified data to the requestor using secure electronic data transmission; the data will then be available for up to 12 months.

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 and gender is reported in the baseline demographics table (Table 1)
Reporting on race, ethnicity, or other socially relevant groupings	Race and ethnicity is reported in the baseline demographics table (Table 1)
Population characteristics	All patients had clinical characteristics typical for resectable pancreatic and colorectal cancer patients. Detailed patient characteristics are provided in Table 1, and Extended Data Table 1.
Recruitment	Complete eligibility and enrollment criteria are provided in the study protocol (Supplementary Materials). Eligible subjects were recruited from 8 centers across diverse geographic regions of the United States. Key eligibility required ECOG performance status 0-1, resectable pancreatic or colorectal cancer, presence of a G12D or G12R somatic KRAS mutation, and positive laboratory evidence of minimal residual disease. Excluded patients had pancreatic neuroendocrine tumors, MSI+ colorectal tumors, other malignancies within the last 3 years anticipated to require treatment, were pregnant or lactating females, or refused to use acceptable methods of contraception. There was no appreciable bias in trial enrollment, and limitations of the small phase 1 population sample are included in the discussion.
Ethics oversight	Two participating institutions, University of Colorado School of Medicine and City of Hope had the study approved by WIRB Copernicus (WCG IRB). Six other participating institutions had the study approved by their local IRBs, Memorial Sloan Kettering Cancer Center (MSKCC IRB), University of Texas MD Anderson (University of Texas MD Anderson Office of Human Subject Protection), University of Iowa (University of Iowa Human Subjects Office/IRB), Northwell Health (Feinstein Institutes for Medical Research, Northwell Health IRB), University of California Los Angeles (UCLA Office of the Human Research Protection Program), and Massachusetts General Hospital (Dana-Farber Cancer Institute Office for Human Research Studies). The study was approved by US FDA and registered on clinicaltrials.gov (NCT04853017).

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	We enrolled 25 patients using an empirical Phase 1 dose escalation design appropriate to evaluate the primary endpoint of safety and as detailed in the study protocol (Supplementary Materials).
Data exclusions	No data were excluded from the analyses. Patient reported outcomes were collected for feasibility but not analyzed in the context of a single arm trial.
Replication	The study findings were reproducible. KRAS mutation status and circulating tumor DNA assays are CLIA validated.
Randomization	Not applicable, because this is a single arm phase 1 clinical trial.
Blinding	Not applicable, because this is an open-label phase 1 clinical trial.

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

Antibodies

Antibodies used

CD4 (BV421, clone: SK3, BD Catalog # 566907, 1:40), CD8 (BV786, clone: RPA-T8, BD Catalog # 563823, 1:25), CD45RA (Alexa 700, clone: HI100, BioLegend Catalog # 304120, 1:25), CCR7 (PE-CF594, clone: 15053, BD Catalog # 562381, 1:12.5), Aqua Live/Dead marker (Thermo Fisher Catalog # L34966, 1:200), CD14 (PE-Cy5, clone: 61D3, Thermo Fisher Catalog # 15-0149-42, 1:200), CD16 (PE-Cy5, clone: 3G8, BioLegend Catalog # 302010, 1:200), and CD19 (PE-Cy5, clone: SJ25C1, BioLegend Catalog # 363042, 1:200), CD3 (APC-H7, clone: SK7, BD Catalog # 560176, 1:40), IFN γ (FITC, clone: Mab11, BioLegend Catalog # 506504, 1:200), TNF α (BV711, clone: B27, BioLegend Catalog # 502940, 1:50), and IL2 (BV650, clone: MQ1-17H12, BioLegend Catalog # 502940, 1:50).

Validation

The specificity of the antibodies purchased from commercial sources (BD Biosciences, BioLegend and Thermo Fisher) were validated by the manufacturer in house.

BD Bioscience:

<https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/quality-and-reproducibility>

1. The specificity is confirmed using multiple methodologies that may include a combination of flow cytometry, immunofluorescence, immunohistochemistry or western blot to test staining on a combination of primary cells, cell lines or transfectant models.

2. All flow cytometry reagents are titrated on the relevant positive or negative cells.

3. Quality control: Quality control testing of new, manufactured lots are performed side-by-side with a previously accepted lot as a control, helping to serve as a reference for comparison and assuring that performance of the new lot is both reliable and consistent.

4. Lot to lot consistency: Testing with prior batches as reference helps you obtain consistent results with the new batch relative to the previous batches.

BioLegend:

<https://www.biolegend.com/en-us/quality/product-development>

Flow cytometry reagents

Specificity testing of 1-3 target cell types with either single or multi-color analysis (including positive and negative cell types). Once specificity is confirmed, each new lot must perform with similar intensity to the in-date reference lot. Brightness (MFI) is evaluated from both positive and negative populations. Each lot product is validated by QC testing with a series of titration dilutions.

Thermo Fisher:

<https://www.thermofisher.com/us/en/home/life-science/antibodies/invitrogen-antibody-validation/relative-expression-antibody-validation.html>

1. Demonstration of primary antibody specificity by relative expression across cell models. Flow cytometry intrinsically facilitates the analysis of relative expression patterns in heterogeneous cell populations. Using gating techniques, verification of antibody binding can be determined by analyzing expression in unique cell types.

2. Independent validated antibodies. Utilizing two independent antibodies for the same protein target can be a useful tool when testing for antibody specificity. In the ideal scenario, two antibodies are used that target nonoverlapping epitopes of an antigen. By obtaining comparable results from antibodies that recognize independent regions of the same target protein, this allows for increased confidence that these antibodies are specific and suitable for the detection of their intended target. Independent antibody testing is one strategy we use to validate Invitrogen antibodies for research use. Common applications of independent antibody validation would be obtaining similar detection patterns in multi-lysate western blots, IHC arrays, immunofluorescence of multiple cell lines, immunoprecipitation, flow cytometry, and other antibody applications.

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 NCT04853017

Study protocol

ELI-002-001 (AMPLIFY-201)

Data collection

The 8 enrolling academic sites were University of Colorado School of Medicine, City of Hope, Memorial Sloan Kettering Cancer Center, University of Texas MD Anderson, University of Iowa, Northwell Health, University of California Los Angeles, and Massachusetts General Hospital. Data were collected from 10 Oct 2021 through 6 September 2023

Outcomes

Safety, tumor biomarker response, relapse free and overall survival were described in the methods.

Flow Cytometry

Plots

Confirm that:

- ☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- ☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- ☒ All plots are contour plots with outliers or pseudocolor plots.
- ☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	PBMCs were processed from leukapheresis using Ficoll-Hypaque gradients or whole blood collection using CPT tubes. PBMCs were cryopreserved and rested overnight before using.
Instrument	BD FACS Symphony
Software	Data was analyzed using FlowJo™ software. Graphs were compiled using GraphPad Prism.
Cell population abundance	No cell sorting was used for the analysis.
Gating strategy	First, a Live-Dead Aqua vs SSC-A gate to exclude non-viable cells, followed by a single cell gate FSC-H vs FSC-A to exclude doublets, then another single cell gate, FSC-A vs FSC-W to further exclude doublets, then a dump negative gate to exclude non T cells followed by FSC-A vs SSC-A to define lymphocytes and a CD3 vs SSC-A to gate on CD3+ T cells. CD4 vs CD8 gate was next used to separate CD8+ cells and CD4+ T cells. For ICS analysis cells, IFN γ , TNF α and IL2 production was then assessed in CD8+ and CD4+ T cells using boolean gating. Memory populations were defined as CCR7 vs CD45RA.

- ☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.