## Experimental design

1. **Sample size**

   Describe how sample size was determined.

   Sample size calculations were not performed. A minimum of 3 replicates were used to establish statistical significance.

2. **Data exclusions**

   Describe any data exclusions.

   No data was excluded.

3. **Replication**

   Describe whether the experimental findings were reliably reproduced.

   All attempts at replication were successful.

4. **Randomization**

   Describe how samples/organisms/participants were allocated into experimental groups.

   No mice or human research participants were used in this study, therefore randomization is not relevant.

5. **Blinding**

   Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

   No mice or human research participants were used in this study, therefore blinding is not relevant.

   Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. **Statistical parameters**

   For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

   n/a  Confirmed

   - [ ] The exact sample size \((n)\) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
   - [ ] A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
   - [ ] A statement indicating how many times each experiment was replicated
   - [ ] The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
   - [ ] A description of any assumptions or corrections, such as an adjustment for multiple comparisons
   - [ ] The test results (e.g. \(P\) values) given as exact values whenever possible and with confidence intervals noted
   - [ ] A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
   - [ ] Clearly defined error bars

   See the web collection on statistics for biologists for further resources and guidance.
Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.

GraphPad Prism was used to analyze dose response curves. Proteomics data was analyzed using Mascot, MaxQuant, Scaffold, ReKINect, NetworKIN, and GEPHI. Cell cycle analysis was done using ModFitLT v3.2.1. Synergy analyses were done using CompuSyn. Network analysis was done using the igraph R package. Custom R code was used for visualization and will be made available upon request.

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). Nature Methods guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.

All unique materials are readily available from the authors.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

All antibody data is provided in the manuscript.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

Cell lines were provided by the Moffitt Cancer Center Lung Cancer Center of Excellence Cell Line Core.

b. Describe the method of cell line authentication used.

All cell lines have been STR verified.

c. Report whether the cell lines were tested for mycoplasma contamination.

All cell lines tested negative for mycoplasma.

d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.

The H157 cell line is reported in the ICLAC database; however, it is only used in this study to demonstrate the range of sensitivity to ceritinib in a large, diverse set of lung cancer cell lines. STR analysis confirm authenticity of these cells.

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

No animals were used.

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

The study did not involve human research participants.
Flow Cytometry Reporting Summary

Data presentation

For all flow cytometry data, confirm that:

1. The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
2. 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).
3. All plots are contour plots with outliers or pseudocolor plots.
4. A numerical value for number of cells or percentage (with statistics) is provided.

Methodological details

5. Describe the sample preparation. Cells were harvested following incubation, fixed with 70% cold ethanol and stored at -20°C until analyzed. Cells were washed with PBS and cell cycle was determined by incubating in a 1 ug/mL DAPI (4', 6-Diamidino-2-phenylindole, Sigma)/0.1% Triton X-100/PBS solution and analyzed by FACS.

6. Identify the instrument used for data collection. FACSCanto II benchtop analyzer (BD Biosciences)

7. Describe the software used to collect and analyze the flow cytometry data. ModFitLT V3.2.1 (Verity Software House); R

8. Describe the abundance of the relevant cell populations within post-sort fractions. n/a

9. Describe the gating strategy used. n/a

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