Supplementary Figure 1. Distribution of cancer types in the study cohort.
LUC, lung cancer; CRC, colorectal cancer; GAC, gastric cancer; BRC, breast cancer; HEPC, hepatobiliary cancer; PAC, pancreatic cancer; OVC, ovarian cancer; STS, soft tissue sarcoma; CEC, cervical cancer; ESC, esophageal cancer; URC, urinary cancer; HNC, head and neck cancer; SKCM, skin cutaneous melanoma; Net, neuroendocrine tumor; PRC, prostate cancer; THC, thyroid cancer
Supplementary Figure 2. Detection of RTK fusions in tumor and cfDNA specimens. A, Heatmaps showing the prevalence of RTK fusions in different cancers comparing tumor specimens and ctDNA samples. B, Bar graph showing similar RTK fusion frequencies between the sample origins, except for a higher prevalence of RET fusion in the ctDNA. The FDR adjusted q values were indicated.
Supplementary Figure 3. Associations of different fusion events with patient sex.

A, ROS1 and ALK fusions showed increased associations with the female sex in the lung cancer cohort. B-D, No associations with sex among different fusion variants of (B) ALK, (C) RET, or (D) ROS1.
Supplementary Figure 4. Associations of different fusion events with patient age.
A, ALK, ROS1 and RET fusions showed increased associations with earlier disease onset in the lung cancer cohort. B, Associations of the ALK v1 variant with younger age and the v3 variant with older age. C-D, No associations with age among different fusion variants of (C) RET or (D) ROS1.
Supplementary Figure 5

A  ALK: Lung

B  ALK: non-lung

C  ALK: Lung EML4-ALK

D  ALK: Lung non-EML4-ALK

E  ALK: Lung EML4-ALK v1

F  ALK: Lung EML4-ALK v3

G

H

I  EML4: Lung ALK fusions

J  non-EML4: Lung ALK fusions
Supplementary Figure 5. Genomic structures of ALK fusions.
A-F, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of the ALK gene in (A) lung cancer, (B) non-lung cancer, (C) EML4-ALK, (D) non-EML4-ALK, (E) EML4-ALK v1 variant, and (F) EML4-ALK v3 variant. G-H, Frequencies of breakpoints in (G) EML4 and (H) other common ALK fusion partners. I-J, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of (I) EML4 and (J) non-EML4 ALK partners.
Supplementary Figure 6. Genomic structures of RET fusions. A-E, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of the RET gene in (A) lung cancer, (B) non-lung cancer, (C) KIF5B-RET, (D) CCDC6-RET, and (E) all other RET fusions. F-H, Frequencies of breakpoints in (F) KIF5B, (G) CCDC6, and (H) NCOA4. I-K, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of (I) KIF5B, (J) CCDC6, and (K) all other RET fusion partners.
Supplementary Figure 7. Consensus plots of ROS1 breakpoints. A-F, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of the ROS1 gene in (A) lung cancer, (B) non-lung cancer, (C) CD74-ROS1, (D) EZR-ROS1, (E) SDC4-ROS1, and (F) other ROS1 fusions.
Supplementary Figure 8. Breakpoint structures of ROS1 fusion partners.
A-B, Frequencies of breakpoints in (A) CD74, (B) other common ROS1 fusion partners. C-F, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of (C) CD74, (D) EZR, (E) SDC4, and (F) all other ROS1 fusion partners.
Supplementary Figure 9. Consensus plots of FGFR family breakpoints. A-D, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of FGFR3 in (A) lung cancer, (B) non-lung cancer, and cases with (C) exon 17 and (D) exon 18 fusions. E, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of TACC3. F-G, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of FGFR2 in (F) gastric cancer and (G) non-gastric cancers. H, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of FGFR2 fusion partners.
Supplementary Figure 10
Supplementary Figure 10. Breakpoint structures of all other common fusions. A-I, consensus plots showing the sequencing patterns ±20 bp around the breakpoints of (A) EGFR in lung cancer, (B) EGFR in non-lung cancer, (C) EGFR fusion partners, (D) ERBB2, (E) ERBB2 fusion partners, (F) MET, (G) MET fusion partners, (H) NTRK and (I) NTRK fusion partners.
Supplementary Figure 11.

Mutational landscape of concomitant mutations comparing lung and non-lung cancers prior to TKI treatment.

Supplementary Figure 11. Mutational landscape of concomitant mutations comparing lung and non-lung cancers prior to TKI treatment.
Supplementary Figure 12

A.

B.

Supplementary Figure 12. Resistance to RTK fusion-targeted therapies
A, mutational landscape of ALK fusion-positive cases pre- and post-TKI treatment. B, An increasing trend towards a higher frequency of subclonal RTK fusions following treatment.
Supplementary Figure 13. Kaplan-Meier estimates of PFS comparing different ALK fusion variants following TKI treatment.

A, Kaplan-Meier estimates of PFS comparing patients with the two major ALK fusion variants following multi-TKI treatment. B, Kaplan-Meier estimates of PFS comparing patients with different ALK fusion variants following crizotinib treatment.
Supplementary Figure 14. IGV showing the breakpoints of the HLA-DRB1-MET fusion.
Supplementary Table 1. Overall frequencies of RTK fusions across different cancer types.

| Cancer Type | ALK | ROS1 | FGFR3 | FGFR2 | FGFR1 | EGF | ERBB2 | ERBB3 | MET | NTRK1 | NTRK3 | PDGFRB | PDGFR | FLT1 | FLT3 | FLT4 | IGFR1 | KDR | EPHA2 | EPHA3 | AXL | KIT | TEK |
|-------------|-----|------|-------|-------|-------|-----|-------|-------|-----|-------|-------|--------|-------|------|------|------|------|------|------|------|------|------|------|------|------|
| PRC (177)   | 7.79| 0.00 | 0.00  | 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PRC (106)   | 1.89| 0.54 | 0.00  | 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| NET (134)   | 3.73| 2.24 | 0.75  | 0.75  | 0.00  | 0.00| 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| HNC (273)   | 0.73| 0.37 | 0.00  | 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| SKCM (276)  | 1.45| 0.00 | 0.36  | 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ESC (336)   | 1.19| 0.00 | 0.30  | 0.00  | 0.60  | 0.00| 0.00  | 0.30  | 0.00| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| CEC (372)   | 1.61| 0.27 | 0.27  | 0.54  | 0.00  | 0.00| 0.00  | 1.08  | 0.27| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| UCEC (417)  | 3.60| 0.00 | 0.24  | 0.24  | 2.16  | 0.72| 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| STS (434)   | 1.38| 0.69 | 0.23  | 0.46  | 0.00  | 0.00| 0.00  | 0.00  | 0.00| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| OVC (494)   | 1.62| 0.61 | 0.20  | 0.40  | 0.00  | 0.00| 0.00  | 0.20  | 0.20| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PAC (538)   | 0.37| 0.00 | 0.19  | 0.00  | 0.00  | 0.00| 0.00  | 0.19  | 0.00| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| HEPG (1,037)| 1.38| 0.10 | 0.00  | 0.00  | 0.29  | 0.49| 0.00  | 0.20  | 0.10| 0.00  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| BRC (1,478) | 1.69| 0.27 | 0.07  | 0.07  | 0.34  | 0.14| 0.20  | 0.27  | 0.00| 0.07  | 0.14  | 0.00   | 0.00  | 0.00 | 0.00 | 0.07 | 0.07 | 0.14 | 0.00 | 0.07 | 0.00 | 0.00 | 0.00 |
| GAC (1,955) | 2.20| 0.15 | 0.10  | 0.05  | 0.20  | 1.18| 0.05  | 0.26  | 0.41| 0.00  | 0.10  | 0.00   | 0.00  | 0.00 | 0.00 | 0.05 | 0.05 | 0.00 | 0.00 | 0.15 | 0.00 | 0.00 | 0.00 |
| CRC (4,130) | 1.02| 0.19 | 0.34  | 0.07  | 0.02  | 0.00| 0.00  | 0.07  | 0.02| 0.12  | 0.00  | 0.00   | 0.00  | 0.00 | 0.00 | 0.02 | 0.02 | 0.01 | 0.00 | 0.02 | 0.00 | 0.00 | 0.00 |
| LUC (16,040)| 7.11| 4.20 | 1.28  | 1.16  | 0.17  | 0.01| 0.02  | 0.11  | 0.07| 0.04  | 0.02  | 0.01   | 0.01  | 0.01 | 0.01 | 0.01 | 0.02 | 0.01 | 0.02 | 0.00 | 0.01 | 0.01 | 0.01 |
| All cancer (28,077)| 4.72| 2.50 | 0.84  | 0.71  | 0.18  | 0.14| 0.04  | 0.11  | 0.13| 0.03  | 0.04  | 0.03   | 0.01  | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |

RTK, receptor tyrosine kinase; LUC, lung cancer; CRC, colorectal cancer; GAC, gastric cancer; BRC, breast cancer; HEPG, hepatobiliary cancer; PAC, pancreatic cancer; OVC, ovarian cancer; STS, soft tissue sarcoma; CEC, cervical cancer; URC, urinary cancer; HNC, head and neck cancer; SKCM, skin cutaneous melanoma; NET, neuroendocrine tumors; PRC, prostate cancer; THC, thyroid cancer.
Supplementary Table 2. Frequencies of RTK fusions across different cancer types in tumor specimens

| All tissue | 100.00 | 57.04 | 16.15 | 14.65 | 2.58 | 1.58 | 0.50 | 1.58 | 1.83 | 0.50 | 0.75 | 0.50 | 0.17 | 0.25 | 0.25 | 0.08 | 0.25 | 0.08 | 0.25 | 0.17 | 0.33 | 0.25 | 0.17 | 0.08 | 0.00 |
|------------|--------|--------|--------|--------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| THC        | 0.67   | 0.00   | 100.00 | 0.00   | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PRC        | 0.08   | 0.00   | 0.00   | 0.00   | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| NET        | 0.33   | 50.00  | 0.00   | 50.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| HNC        | 0.17   | 100.00 | 0.00   | 0.00   | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| SKCM       | 0.33   | 0.00   | 50.00  | 50.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ESC        | 0.17   | 0.00   | 50.00  | 0.00   | 50.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| CEC        | 0.58   | 14.29  | 0.00   | 0.00   | 28.57 | 0.00 | 0.00 | 0.00 | 57.14 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| URC        | 1.17   | 0.00   | 7.14   | 14.29  | 50.00 | 14.29 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| STS        | 0.58   | 71.43  | 14.29  | 14.29  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| OVC        | 0.67   | 37.50  | 12.50  | 12.50  | 0.00 | 0.00 | 0.00 | 12.50 | 12.50 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PAC        | 0.17   | 0.00   | 50.00  | 0.00   | 0.00 | 0.00 | 0.00 | 50.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| HEPC       | 1.08   | 7.69   | 0.00   | 0.00   | 23.08 | 38.46 | 0.00 | 0.00 | 7.69 | 0.00 | 23.08 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| BRC        | 1.50   | 11.11  | 5.56   | 0.00   | 0.00 | 27.78 | 5.56 | 11.11 | 5.56 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GAC        | 2.08   | 8.00   | 0.00   | 0.00   | 4.00 | 20.00 | 0.00 | 16.00 | 24.00 | 0.00 | 8.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 12.00 | 0.00 | 0.00 |
| CRC        | 2.58   | 16.13  | 32.26  | 6.45   | 3.23 | 0.00 | 6.45 | 3.23 | 6.45 | 0.00 | 12.90 | 0.00 | 3.23 | 3.23 | 0.00 | 3.23 | 0.00 | 3.23 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LUC        | 87.84  | 62.75  | 16.11  | 15.83  | 1.52 | 0.09 | 1.94 | 0.47 | 1.57 | 0.19 | 0.19 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 |

RTK, receptor tyrosine kinase; LUC, lung cancer; CRC, colorectal cancer; GAC, gastric cancer; BRC, breast cancer; HEPC, hepatobiliary cancer; PAC, pancreatic cancer; OVC, ovarian cancer; STS, soft tissue sarcoma; CEC, cervical cancer; ESC, esophageal cancer; URC, urinary cancer; HNC, head and neck cancer; SKCM, skin cutaneous melanoma; NET, neuroendocrine tumors; PRC, prostate cancer; THC, thyroid cancer
## Supplementary Table 3. Frequencies of RTK across different cancer types in cfDNA samples.

| All cfDNA | THC | PRC | NET | HNC | SKCM | ESC | CEC | URC | STS | PAC | OVC | NET | BRC | CRC | LUC |
|-----------|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 100.00    | 84.22 | 2.13 | 0.43 | 0.21 | 0.43 | 0.43 | 0.00 | 0.21 | 0.43 | 0.43 | 0.43 | 0.43 | 0.43 | 0.43 | 0.43 | 0.43 |
| ALK       | 55.44 | 10.00 | 11.51 | 0.00 | 11.11 | 0.00 | 0.00 | 0.00 | 0.21 | 0.00 | 0.00 | 11.11 | 0.00 | 5.56 | 2.00 | 0.00 |
| FGFR3     | 5.56  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| FGFR2     | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| FGFR1     | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| EGF       | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| EGFR      | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| BRB2      | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| BRB3      | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| NTRK1     | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| NTRK3     | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| PDGFRB    | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| PDGFB     | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| FLT1      | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| FLT4      | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| IFGFR1    | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| KDR       | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| EPHA2     | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| EPHA3     | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| AXL       | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |
| TRK       | 0.00  | 0.00  | 0.00  | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00  | 0.00 | 0.00 | 0.00 | 0.00 |

RTK, receptor tyrosine kinase; LUC, lung cancer; CRC, colorectal cancer; GAC, gastric cancer; BRC, breast cancer; HEPC, hepatobiliary cancer; PAC, pancreatic cancer; OVC, ovarian cancer; STS, soft tissue sarcoma; CEC, cervical cancer; ESC, esophageal cancer; URC, urinary cancer; HNC, head and neck cancer; SKCM, skin cutaneous melanoma; NET, neuroendocrine tumors; PRC, prostate cancer; THC, thyroid cancer
Supplementary Table 4. Concomitant driver mutations in RTK fusion carriers

| Patient ID | Cancer type | Fusion RTK | Fusion gene       | Clonality of fusion gene | concomitant driver gene | Driver mutation | Clonality of concomitant drivers |
|------------|-------------|------------|-------------------|--------------------------|--------------------------|----------------|---------------------------------|
| PT242      | Lung        | ALK        | EML4-ALK V1       | clonal                   | KRAS                     | Q65H           | subclonal                       |
| PT852      | Lung        | ALK        | EML4-ALK V3       | clonal                   | BRCA2                    | G267fs         | subclonal                       |
| PT1293     | Lung        | ALK        | ARMCR9-ALK        | clonal                   | BRCA2                    | Q3047*          | clonal                          |
| PT504      | Lung        | ALK        | EML4-ALK V1       | clonal                   | PTEN                     | E288fs         | clonal                          |
| PT390      | Lung        | RET        | KIF5B-RET         | subclonal                | NRAS                     | G12D           | subclonal                       |
| PT787      | Lung        | RET        | CDDC6-RET         | subclonal                | EGFR                     | E7T30delinsD (exon 18) | subclonal |
| PT1309     | Lung        | RET        | VSTM4-RET         | clonal                   | EGFR                     | E858R          | clonal                          |
| PT750      | Lung        | RET        | DCLRE1C-RET       | subclonal                | EGFR                     | N771delinsNG (exon 20) | subclonal |
| PT246      | Lung        | RET        | KIF5B-RET         | clonal                   | BRCA1                    | E670fs         | subclonal                       |
| PT36       | Lung        | RET        | KIF5B-RET         | clonal                   | PTEN                     | V317fs         | subclonal                       |
| PT500      | Lung        | RET        | CDDC6-RET         | subclonal                | PTEN                     | D22fs          | subclonal                       |
| PT576      | CRC         | ROS1       | GOPC-ROS1         | subclonal                | BRCA2                    | T3030fs        | subclonal                       |
| PT790      | Lung        | ROS1       | SDG4-ROS1         | subclonal                | PIK3CA                   | H1047R         | subclonal                       |
| PT1266     | Hepatobiliary | FGFR2    | FGFR2-PROB1       | clonal                   | NRAS                     | G12V           | subclonal                       |
| PT896      | Breast      | FGFR2      | FGFR2-SHTN1       | clonal                   | PIK3CA                   | H1047R         | clonal                          |
| PT535      | Lung        | FGFR3      | FGFR3-TACC3       | clonal                   | KRAS                     | G13D           | subclonal                       |
| PT783      | Gastric     | FGFR3      | FGFR3-TACC3       | subclonal                | KRAS                     | A146V          | subclonal                       |
| PT518      | Ovarian     | MET        | Slc25A19-MET      | clonal                   | KRAS                     | Q61R           | subclonal                       |
| PT512      | Ovarian     | MET        | Slc25A19-MET      | clonal                   | KRAS                     | G12V           | clonal                          |