**Table S1. MERTK targeting agents in clinical development.**

| Agent name | Therapeutic modality | Targets | Interventions | Malignancies targeted | Development phase | Trial ID ; Status |
|---|---|---|---|---|---|---|
| MRX-2843 | Small-molecule kinase inhibitor | MERTK, FLT3, AXL, TRKA, LOK | Monotherapy | Advanced solid tumors | Phase I | NCT03510104 ; Completed |
| | | | Monotherapy | R/R AML, ALL, or MPAL | Phase I | NCT04872478 ; Recruiting |
| | | | In combination with osimertinib (EGFR TKI) | EGFR-mutant NSCLC | Phase I | NCT04762199 ; Recruiting |
| ONO-7475 | Small-molecule kinase inhibitor | MERTK, AXL | Monotherapy or in combination with nivolumab (anti-PD-1 antibody) | Advanced or metastatic solid tumors | Phase I | NCT03730337 ; Completed |
| Q702 | Small-molecule kinase inhibitor | AXL, MERTK, CSF1R | Monotherapy | Advanced solid tumors | Phase I | NCT04648254 ; Recruiting |
| | | | In combination with pembrolizumab (anti-PD1 antibody) | Advanced esophageal, gastric/GEJ, hepatocellular, and cervical cancers | Phase I/II | NCT05438420 ; Recruiting |
| | | | In combination with azacitidine and venetoclax | R/R AML | Phase I | NCT06445907 ; Not yet recruiting |
| PF-07265807 | Small-molecule kinase inhibitor | AXL, MERTK | Monotherapy | Advanced or metastatic solid tumors | Phase I | NCT04458259 ; Active, not recruiting |
| | | | In combination with sasanlimab (anti-PD-1 antibody) | | | |
| | | | In combination with sasanlimab and axitinib (VEGFR TKI) | | | |
| INCB081776 | Small-molecule kinase inhibitor | AXL, MERTK, MET | Monotherapy or in combination with retifanlimab (anti-PD-1 antibody) | Advanced or metastatic solid tumors , R/R AML | Phase I | NCT03522142 ; Active, not recruiting |
| | | | In combination with pembrolizumab (anti-PD-1 antibody) and palliative radiation therapy | Recurrent/metastatic HNSCC | Phase I | NCT06308913 ; Recruiting |
| RXDX-106 | Small-molecule kinase inhibitor | AXL,TYRO3, MET, MERTK, RON, ABL1, LCK, TRKA/C | Monotherapy | Advanced or metastatic solid tumors | Phase I | NCT03454243 ; Terminated |
| BMS-777607 (ASLAN002) | Small-molecule kinase inhibitor | AXL, RON, MET, TYRO3, MERTK, FLT3, AURKB, LOK, TIE2, MKNK2, MUSK | Monotherapy | Advanced or metastatic solid tumors | Phase I/II | NCT00605618 ; Completed |
| | | | Monotherapy | Advanced or metastatic solid tumors | Phase I | NCT01721148 ; Completed |
| XL092 | Small-molecule kinase inhibitor | MET, VEGFR2, MER, AXL | In combination with atezolizumab (anti-PD-L1 antibody) | Metastatic colorectal cancer | Phase III | NCT05425940 ; Recruiting |
| | | | In combination with nivolumab (anti-PD-1 antibody) | Advanced or metastatic nccRCC | Phase III | NCT05678673 ; Recruiting |
| | | | Monotherapy or in combination with atezolizumab (anti-PD-L1 antibody) or in combination with avelumab (anti-PD-L1 antibody) | Advanced solid tumors | Phase I | NCT03845166 ; Active, not recruiting |
| | | | In combination with nivolumab (anti-PD-1 antibody) or in combination with ipilimumab (anti-CTLA4 antibody) and nivolumab or in combination with nivolumab + relatlimab (anti-LAG-3 antibody) | Advanced solid tumors | Phase I | NCT05176483 ; Recruiting |
| | | | In combination with AB521(HIF-2α inhibitor) or in combination with AB521 and nivolumab (anti-PD-1 antibody) | Advanced ccRCC or other advanced solid tumors | Phase I | NCT06191796; Recruiting |
| | | | In combination with pembrolizumab (anti-PD-1 antibody) | PD-L1 positive recurrent or metastatic HNSCC | Phase II/III | NCT06082167; Recruiting |
| | | | In combination with atezolizumab (anti-PD-L1 antibody) and tiragolumab (anti-TIGIT antibody) | Metastatic NSCLC | Phase I/II | NCT03337698 ; Active, not recruiting |
| Merestinib (LY2801653) | Small-molecule kinase inhibitor | MERTK, DDR1, AXL, MKNK1/2, FLT3, DDR2, RON, ROS1, TYRO3, MET, PDGFRA, TEK | In combination with LY2874455 (FGFR TKI) | R/R AML | Phase I | NCT03125239 ; Completed |
| | | | Monotherapy or in combination with cisplatin and gemcitabine | Advanced and/or metastatic solid tumors or non-Hodgkin's lymphoma | Phase I | NCT03027284 ; Completed |
| | | | In combination with cisplatin and gemcitabine | Advanced or metastatic biliary tract cancer | Phase II | NCT02711553 ; Active, not recuriting |
| | | | In combination with ramucirumab (anti-VEGFR-2 antibody) | Advanced or metastatic colorectal cancer, MCL | Phase I | NCT02745769 ; Completed |
| | | | Monotherapy or in combination with cetuximab (anti-EGFR antibody) or in combination with cisplatin or in combination with cisplatin and gemcitabine or in combination with ramucirumab (anti-VEGFR-2 antibody) | Advanced cancer | Phase I | NCT01285037; Completed |
| | | | In combination with LY3300054 (anti-PD-L1 antibody) | Pancreatic cancer | Phase I | NCT02791334 ; Active, not recuriting |
| Ningetinib (CT053PTSA) | Small-molecule kinase inhibitor | c-Met, VEGFR2, AXL, MERTK, and FLT3 | Monotherapy | Advanced NSCLC | Phase II | NCT04992858 ; Not yet recruiting |
| | | | Monotherapy | Advanced solid tumors | Phase I | NCT04577703 ; Completed |
| AT9283 | Small-molecule kinase inhibitor | AURKA/B, JAK2/3, ABL1, MERTK, GSK3β, FGFR2, VEGFR3, RET, RSK2/3, TYK2, YES, FLT3, DRAK1, FGFR1/3, VEGFR1/2, PDGFRA, PDK1 | Monotherapy | Multiple myeloma | Phase II | NCT01145989 ; Completed |
| | | | Monotherapy | Advanced or metastatic solid tumors or non-Hodgkin's lymphoma | Phase I | NCT00443976 ; Completed |
| | | | Monotherapy | R/R acute leukemias | Phase I | NCT01431664 ; Completed |
| | | | Monotherapy | R/R solid tumors | Phase I | NCT00985868 ; Completed |
| Foretinib | Small-molecule kinase inhibitor | AXL, MET, MERTK, VEGFR2/3, TIE2, TYRO3, RON, FLT3, PDGFRA, VEGFR1, KIT, PDGFRB, ROS1 | Monotherapy | Hepatocellular carcinoma | Phase I | NCT00920192 ; Completed |
| | | | Monotherapy | Breast cancer | Phase II | NCT01147484 ; Completed |
| | | | In combination with lapatinib (EGFR/HER2 TKI) | Breast cancer | Phase I/II | NCT01138384 ; Completed |
| | | | Monotherapy | Solid tumors | Phase I | NCT00742131 ; Completed |
| | | | Monotherapy | Head and neck cancer | Phase II | NCT00725764 ; Completed |
| | | | Monotherapy | Papillary renal cell carcinoma | Phase II | NCT00726323 ; Completed |
| | | | Monotherapy | Solid tumors | Phase I | NCT00742261 ; Completed |
| | | | Monotherapy | Metastatic gastiric cancer | Phase II | NCT00725712 ; Completed |
| | | | Monotherapy | Solid tumors | Phase I | NCT00743067 ; Completed |
| | | | In combination with erlotinib (EGFR TKI) | Advanced or metastatic NSCLC | Phase I/II | NCT01068587 ; Completed |
| S49076 | Small-molecule kinase inhibitor | MET, AXL, FGFR1/2/3 | Monotherapy | Advanced solid tumors | Phase I | ISRCTN00759419; Completed |
| | | | In combination with bevacizumab (anti-VEGF antibody) | GBM | Phase I/II | EudraCT2013-003079-37 or ISRCTN11619481; Completed |
| | | | In combination with gefitinib (EGFR TKI) | NSCLC | Phase I/II | EudraCT2015-002646-31 ; Completed |
| Sitravatinib | Small-molecule kinase inhibitor | DDR2, EPHA3, AXL, MERTK, TYRO3, FLT3, VEGFR, PDGFR, KIT, MET, RET, TRKA, TRKB | Monotherapy | Advanced liposarcoma and other soft tissue sarcomas | Phase II | NCT02978859 ; Active, not recruiting |
| | | | In combination with tislelizumab (anti-PD-1 antibody) | HCC | Phase II | NCT05407519 ; Recruiting |
| | | | In combination with tislelizumab (anti-PD-1 antibody) | Advanced biliary tract cancer | Phase II | NCT04727996; Active, not recruiting |
| | | | In combination with nivolumab (anti-PD-1 antibody) | Metastatic or advanced ccRCC | Phase II | NCT04904302; Active, not recruiting |
| | | | In combination with tislelizumab (anti-PD-1 antibody) | ES-SCLC | Phase II | NCT05228496; Active, not recruiting |
| | | | In combination with tislelizumab (anti-PD-1 antibody) or in combination with tislelizumab and nab-paclitaxel | Recurrent or metastatic TNBC | Phase II | NCT04734262; Active, not recruiting |
| | | | In combination with tislelizumab (anti-PD-1 antibody) | Metastatic uveal melanoma | Phase II | NCT05542342; Active, not recruiting |
| | | | Monotherapy | NSCLC | Phase II | NCT02664935; Active, not recruiting |
| | | | In combination with nivolumab (anti-PD-1 antibody) | Advanced non-squamous NSCLC | Phase III | NCT03906071; Active, not recruting |
| | | | Monotherapy or in combination with other anitcancer therapies | Advanced or metastatic solid malignancies | Phase II/III (as extension of parent clinical trial) | NCT04887870 (Extension trial) ; Active, not recruting |
| | | | Monotherapy or in combination with tislelizumab (anti-PD-1 antibody) | Advanced malignancies | Phase III (as extension of parent clinical trial) | NCT04164199 (Extenstion trial) ; Enrolling by invitation |
| SLC-391 | Small-molecule kinase inhibitor | AXL, FGFR3, VEGFR, MERTK, TYRO3, FGFR2, ALK | Monotherapy | Solid tumors | Phase I | NCT03990454 ; Completed |
| | | | In combination with pembrolizumab (anti-PD1 antibody) | Advanced or metastatic NSCLC | Phase I/II | NCT05860296 ; Recruiting |

For each agent, all active or completed (non-terminated) clinical trails in cancer patients have been included except for S49076, sitravatinib, and RXDX-106. Listed trials are the only known trials for RXDX-106. As S49076 clinical trails are not listed in www.clinicaltrials.gov, a more comprehensive trial list for this agent could not be formulated. For sitravatininb, only active trails are included in the interest of brevity. For a more comprehensive list visit : www.clinicaltrials.gov

ALL, acute lymphoid leukemia; AML, acute myeloid leukemia; ccRCC, clear cell renal cell carcinoma; CML, chronic myeloid leukemia; ES-SCLC, extensive stage small cell lung cancer; GBM, glioblastoma multiforme; GEJ, gastroesophageal junction; HNSCC, head and neck squamous cell carcinoma; MCL, mantle cell lymphoma ; MDS, myelodysplastic syndrome; MPAL, mixed-phenotype acute leukemia; nccRCC, non-clear cell renal cell carcinoma; NSCLC, non-small-cell lung cancer; R/R, relapsed refractory; TNBC, triple negative breast cancer; TKI, tyrosine kinase inhibitor