

Supplementary Table S1. Clinical studies of combination therapy for cancer treatment

Combination studies	Phase	Cancer type	Registration number	Status	Inventors
DNX2401 Temozolomide	I	Glioblastoma multiforme Recurrent tumor	NCT01956734	Completed	Clinica universidad de Navarra
CVA21 Ipilimumab	I	Uveal melanoma Liver metastases	NCT03408587	Completed	Icahn school of medicine at Mount Sinai
Pexa-Vec Ipilimumab	I	Metastatic tumor Advanced tumor	NCT02977156	Completed	Centre Leon Berard
GL-ONC1 Radiation Cisplatin	I	Head and neck cancer	NCT01584284	Completed	Moore's UC San Diego cancer center
REOLYSIN® Irinotecan Leucovorin Fluorouracil (5-FU) Bevacizumab	I	KRAS mutant metastatic colorectal cancer	NCT01274624	Completed	Oncolytics biotech and montefiore medical center
REOLYSIN® Gemcitabine Irinotecan Leucovorin 5-fluorouracil Pembrolizumab	I	Pancreatic adenocarcinoma	NCT02620423	Completed	Cancer therapy and research center at UTHSCSA
GL-ONC1 Bevacizumab	I/II	Ovarian cancer Peritoneal carcinomatosis Fallopian tube cancer	NCT02759588	Completed	Genelux corporation
Ad-MAGEA3 MG1-MAGEA3 Pembrolizumab	I/II	Non-small cell lung cancer	NCT02879760	Completed	Turnstone biologics, Corp.
TBI-1401(HF10) Ipilimumab	II	Melanoma stage III Melanoma stage IV	NCT03153085	Completed	National cancer center hospital
DNX-2401 Pembrolizumab	II	Brain cancer Brain neoplasm Glioma Glioblastoma Gliosarcoma Malignant brain tumor Neoplasm, Neuroepithelial neuroectodermal tumors	NCT02798406	Completed	DNAtrix, Inc.

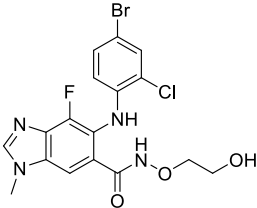
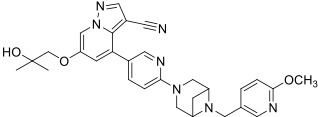
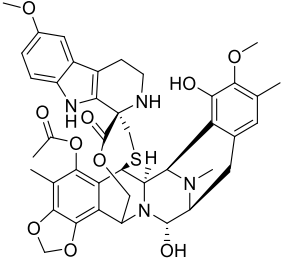
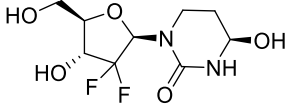
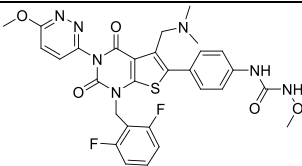
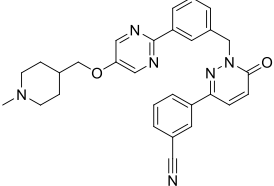
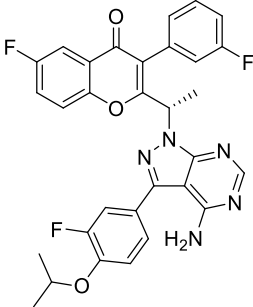
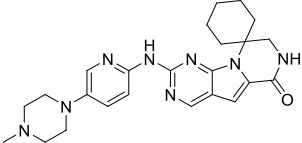
		Neoplasm by histologic type Nerve tissue nervous system diseases			
HF10 Ipilimumab	II	Malignant melanoma	NCT02272855	Completed	University of Utah
RT-01 Nivolumab	I	Advanced solid tumor	NCT05228119	Recruiting	The affiliated hospital of Xuzhou medical university
RT-01 Nivolumab	I	Advanced solid tumor	NCT05122572	Recruiting	Wuxi People's hospital
ASP9801 Pembrolizumab	I	Metastatic cancer Solid tumor Advanced cancer	NCT03954067	Recruiting	Astellas pharma global development, Inc.
RP3 Nivolumab	I	Advanced solid tumor	NCT04735978	Recruiting	Replimune Inc.
Enadenotucirev Capecitabine Radiotherapy	I	Locally advanced rectal cancer	NCT03916510	Recruiting	University of Oxford
TILT-123 Avelumab	I	Melanoma Head and neck squamous cell Carcinoma	NCT05222932	Recruiting	Docrates cancer center
OVV-01 injection Pembrolizumab	I	Neoplasms	NCT04787003	Recruiting	North China petroleum bureau general hospital
TBio-6517 Pembrolizumab	I/II	Solid tumor Microsatellite stable colorectal cancer HPV-positive oropharyngeal squamous cell carcinoma Cervical cancer Melanoma (skin) Cutaneous squamous cell carcinoma Mesothelioma Renal cell carcinoma Oropharynx cancer	NCT04301011	Recruiting	Turnstone biologics
Delolimogene Mupadenorepvec Gemcitabine	I/II	Pancreatic cancer	NCT02705196	Recruiting	Lokon pharma AB

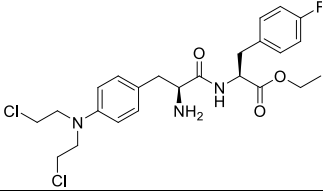
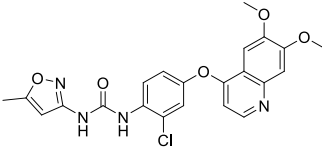
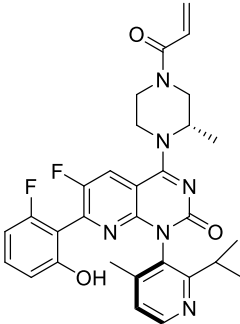
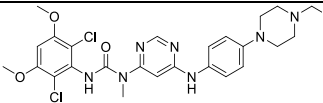
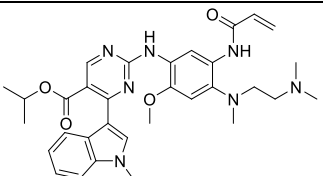
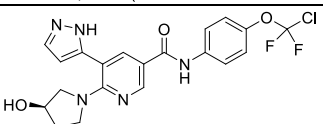
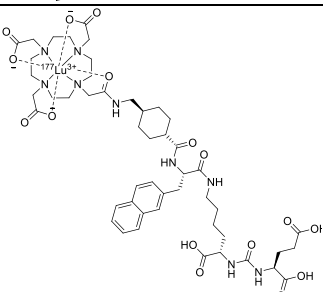
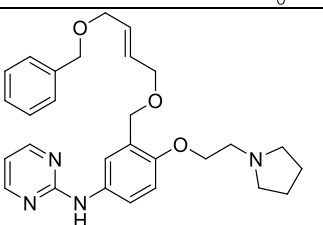
Nab-Paclitaxel Atezolizumab					
Olvimulogene Nanivacirepvec Pcarboplatin (preferred) or Cisplatin Gemcitabine, Taxane (Paclitaxel, Docetaxel or Nab-Paclitaxel) or Pegylated liposomal Doxorubicin Bevacizumab	III	Platinum-resistant ovarian cancer Platinum-refractory ovarian cancer Fallopian tube cancer Primary peritoneal cancer High-grade serous ovarian cancer Endometrioid ovarian cancer Ovarian clear cell carcinoma	NCT05281471	Recruiting	Genelux corporation GOG foundation
MEDI5395 Durvalumab	I	Advanced solid tumors	NCT03889275	Active not recruiting	MedImmune LLC
ONCR-177 Pembrolizumab	I	Melanoma Solid tumor Squamous cell carcinoma of head and neck Breast cancer Advanced solid tumor Triple negative breast cancer Colorectal carcinoma Non-melanoma skin cancer Liver metastases	NCT04348916	Active not recruiting	Oncorus, Inc.
ADV/HSV-tk Valacyclovir Stereotactic body radiation therapy Pembrolizumab	I	Metastatic non-small cell lung cancer Metastatic triple- negative breast cancer	NCT03004183	Active not recruiting	Houston methodist cancer center
TBI-1401(HF10) Gemcitabine Nab-paclitaxel TS-1	I	Pancreatic cancer stage III Pancreatic cancer stage IV	NCT03252808	Active not recruiting	Takara Bio Inc.
Pexastimogene Devacirepvec (Pexa- Vec) Cemiplimab	I/II	Renal cell carcinoma	NCT03294083	Active not recruiting	SillaJen, Inc. Regeneron pharmaceuticals
Talimogene laherparepvec Paclitaxel	I/II	Ductal carcinoma Invasive breast carcinoma Invasive ductal breast carcinoma	NCT02779855	Active not recruiting	H. Lee Moffitt cancer center and research institute

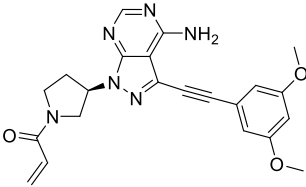
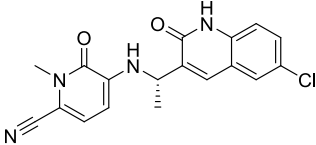
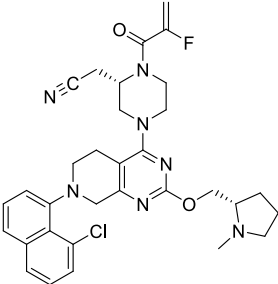
Durvalumab Tremelimumab Pexa-Vec	I/II	Colorectal cancer Colorectal carcinoma Colorectal adenocarcinoma Refractory cancer Colorectal neoplasms	NCT03206073	Active not recruiting	National cancer institute (NCI)
Paclitaxel Pelareorep Avelumab	II	Breast cancer metastatic	NCT04215146	Active not recruiting	Oncolytics biotech PrECOG, LLC.
Recombinant oncolytic HSV-2 Recombinant humanized anti-PD-1 mAb Radiation	I	Melanoma stage IV	NCT05068453	Not yet recruiting	Peking university cancer hospital & institute
Recombinant oncolytic HSV-2 Axitinib	I	Melanoma stage IV	NCT05070221	Not yet recruiting	Peking university cancer hospital & institute
Revottack PD-1	I	Advanced solid tumor	NCT05644509	Not yet recruiting	The affiliated hospital of Xuzhou medical university
G207 Radiation (5 Gy single dose)	II	High-grade glioma Glioblastoma multiforme Malignant glioma of the brain Anaplastic astrocytoma of the brain High-grade glioma Anaplastic glioma Giant cell glioblastoma	NCT04482933	Not yet recruiting	University of Alabama at Birmingham
Lenalidomide or Pomalidomide REOLYSIN	I	Multiple myeloma	NCT03015922	Unknown	St. James's university hospital
TG6002 5-flucytosine	I/II	Glioblastoma Brain cancer	NCT03294486	Unknown	Assistance Publique - Hôpitaux de Paris
H101 Radiation	-	Genital neoplasms	NCT05051696	Enrolling by invitation	First affiliated hospital Xi'an Jiaotong university

Supplementary Table S2. Recent FDA-approved small molecules targeting essential pathways for cancer treatment

Drug name	Active small molecule	Structure	Target	Cancer type	Approval date
Balversa	Erdafitinib		pan-EGFR inhibitor	Advanced and metastatic bladder cancer	4/12/2019
Piqray	Alpelisib		PI3K- α inhibitor	Breast cancer	5/24/2019
Xpovio	Selinexor		XPO1 inhibitor	Relapsed and refractory myeloma	7/3/2019
Nubeqa	Darolutamide		AR antagonist	Non-metastatic castration resistant prostate cancer	07/30/2019
Turalio	Pexidartinib		CSF1R inhibitor	Symptomatic tenosynovial giant cell tumor	08/02/2019
Rozlytrek	Entrectinib		ROS1/TRK/ALK inhibitor	Metastatic non-small cell lung cancer	08/15/2019
Inrebic	Fedratinib		JAK-2 inhibitor	High-risk primary and secondary myelofibrosis	08/16/2019
Brukina	Zanubrutinib		BTK inhibitor	Mantle cell lymphoma	11/14/2019
Tazverik	Tazemetostat		EZH2 methyl transferase inhibitor	Epitheloid carcinoma	1/23/2020

Koselgo	Selumetinib		MEK1/MEK2 kinase inhibitor	Neurofibromatosis type 1	4/10/2020
Retevmo	Selpercatinib		RET fusion kinase Inhibitor	NSCLC, Thyroid cancer	5/8/2020
Zepzelca	Iurbinectedin		DNA alkylating agent	Metastatic small cell lung cancer	6/15/2020
Inqovil	Cedazuridine/ Decitabine		Nucleoside cytidine deaminase inhibitor	Myelodysplastic syndromes	7/7/2020
Orgovyx	Relugolix		GnRH hormone receptor antagonist	Advanced prostate cancer	12/18/2020
Tepmetko	Tepotinib		MET kinase inhibitor	NSCLC	2/3/2021
Ukoniq	Umbralisib		PI3Kδ and CK1ε Kinase inhibitor	Follicular lymphoma	2/5/2021
Cosela	Trilaciclib		CDK-4 and CDK-5 Kinase inhibitor	SCLC	2/12/2021

Pepaxto	Melphalan-flufenamide		Conjugated alkylating agent	Multiple myeloma	2/26/2021
Fotivda	Tivozanib		Pan-VEGFR kinase inhibitor	Renal cell carcinoma	3/10/2021
Lumakras	Sotorasib		KRAS GTPase inhibitor	NSCLC	5/21/2021
Truseltiq	Infigratinib		Pan-FGFR kinase inhibitor	Cholangiocarcinoma	5/28/2021
Exkivity	Mobocertinib		EGF R exon 20 insertion kinase inhibitor	NSCLC	9/15/2021
Scemblix	Asciminib		ABL/BCR-ABL1 kinase inhibitor	Myeloid leukemia	10/29/2021
Pluvicto	Lutetium (177Lu) vipivotide tetraxetan		PSMA targeted radiotherapy	Prostate cancer	3/23/2022
Vonjo	Pacritinib		JAK-2/IRAK1 inhibitor	Myelofibrosis	2/28/2022

Lytgobi	Futibatinib		FGFR2 inhibitor	Intrahepatic cholangiocarcinoma	9/30/2022
Rezlidhia	Olutasidenib		IDG1 inhibitor	Relapsed/ refractory acute myeloid leukemia	12/1/2022
Krazati	Adagrasib		KRAS inhibitor	Advanced or metastatic NSCLC	12/12/2022