Supplementary Table S2: Molecular Targets detected in our analysis (classified as TIER IIC) and the relative clinical trials (ongoing or completed)

Molecular target	NCT ID (Status)	Study title	Experimental drug [definition]	FDA/EMA-approval
CDK4/6 – CCND3	NCT04116541 (recruiting)	A Study Evaluating the Activity of Anti-cancer Treatments Targeting Tumor Molecular Alterations/Characteristics in Advanced / Metastatic Tumors (MegaMOST)	Ribociclib (plus HDM201) [CDK-inhibitor]	Breast Cancer
CDK4/6 – CCND3	NCT04594005 (active)	CDK4/6 Tumor, Abemaciclib, Paclitaxel	Abemaciclib (plus paclitaxel) [CDK-inhibitor]	Breast Cancer
CDK4/6 – CCND3	NCT03310879 (recruiting)	Study of the CDK4/6 Inhibitor Abemaciclib in Solid Tumors Harboring Genetic Alterations in Genes Encoding D-type Cyclins or Amplification of CDK4 or CDK6	Abemaciclib [CDK-inhibitor]	Breast Cancer
CDK4/6	NCT02693535 (recruiting)	TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)	Abemaciclib [CDK-inhibitor]	Breast Cancer
CDK4/6	NCT03239015 (unknown)	Efficacy and Safety of Precision Therapy in Refractory Tumor	Palbociclib [CDK-inhibitor]	Breast Cancer
CDK4	NCT03297606 (recruiting)	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR) (CAPTUR)	Palbociclib [CDK-inhibitor]	Breast Cancer
CDK4/6	NCT02693535 (recruiting)	TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)	Palbociclib [CDK-inhibitor]	Breast Cancer
BRCA1 – CHEK2 - RAD51C – RAD54L	NCT04123366 (active)	Study of Olaparib (MK-7339) in Combination With Pembrolizumab (MK-3475) in the Treatment of Homologous Recombination Repair Mutation (HRRm) and/or Homologous Recombination Deficiency (HRD)-Positive Advanced Cancer (MK-7339-007/KEYLYNK-007)	Olaparib (plus pembrolizumab) [PARPi]	Ovary, fallopian tubes, peritoneum cancers; breast cancer; pancreatic cancer; prostate cancer
BRCA1 – CHEK2 - RAD51C – RAD54L	NCT03742895 (recruiting)	Efficacy and Safety of Olaparib (MK-7339) in Participants With Previously Treated, Homologous Recombination Repair Mutation (HRRm) or Homologous Recombination Deficiency (HRD) Positive Advanced Cancer (MK-7339-002 / LYNK-002)	Olaparib [PARPi]	Ovary, fallopian tubes, peritoneum cancers; breast cancer; pancreatic cancer; prostate cancer

BRCA1	NCT03239015 (unknown)	Efficacy and Safety of Precision Therapy in Refractory Tumor	Olaparib [PARPi]	Ovary, fallopian tubes, peritoneum cancers; breast cancer; pancreatic cancer; prostate cancer
BRCA1	NCT06065059 (recruiting)	Study to Evaluate TNG348 Alone and With a PARP Inhibitor in Patients With BRCA 1/2 Mutant or HRD+ Solid Tumors	Olaparib (plus TNG348) [PARPi]	Ovary, fallopian tubes, peritoneum cancers; breast cancer; pancreatic cancer; prostate cancer
BRCA1	NCT03297606 (recruting)	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR) (CAPTUR)	Olaparib [PARPi]	Ovary, fallopian tubes, peritoneum cancers; breast cancer; pancreatic cancer; prostate cancer
BRCA1	NCT01078662 (active)	Open Label Study to Assess Efficacy and Safety of Olaparib in Confirmed Genetic BRCA1 or BRCA2 Mutation Pats	Olaparib [PARPi]	Ovary, fallopian tubes, peritoneum cancers; breast cancer; pancreatic cancer; prostate cancer
BRCA1	NCT02338622 (completed)	Trial of Olaparib in Combination With AZD5363 (ComPAKT) (ComPAKT)	Olaparib (plus AZD5363) [PARPi]	Ovary, fallopian tubes, peritoneum cancers; breast cancer; pancreatic cancer; prostate cancer
BRCA1	NCT02693535 (recruiting)	TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)	Olaparib [PARPi]	Ovary, fallopian tubes, peritoneum cancers; breast cancer; pancreatic cancer; prostate cancer
BRCA1	NCT02358200 (terminated)	Study of BMN-673 With Carboplatin and Paclitaxel in Patients With Advanced BRCA-mutated Solid Tumor or Triple Negative Metastatic Breast Cancer	Talazoparib (plus paclitaxel/carboplatin) [PARPi]	Breast cancer

BRCA1 – CHEK2 – MLH1	NCT02693535 (recruiting)	TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)	Talazoparib (plus atezolizumab) [PARPi]	Breast cancer
BRCA1	NCT05097599 (recruiting)	Strata PATH™ (Precision Indications for Approved Therapies) (Strata PATH)	Talazoparib [PARPi]	Breast cancer
BRCA1	NCT03565991 (terminated)	Javelin BRCA/ATM: Avelumab Plus Talazoparib in Patients With BRCA or ATM Mutant Solid Tumors	Talazoparib (plus avelumab) [PARPi]	Breast cancer
BRCA1	NCT02358200 (terminated)	Study of BMN-673 With Carboplatin and Paclitaxel in Patients With Advanced BRCA-mutated Solid Tumor or Triple Negative Metastatic Breast Cancer	Talazoparib (plus paclitaxel/carboplatin) [PARPi]	Breast cancer
BRCA1 – CHEK2 – MLH1	NCT02693535 (recruiting)	TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)	Talazoparib (plus atezolizumab) [PARPi]	Breast cancer
BRCA1	NCT04591431 (active)	The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy (ROME)	Talazoparib [PARPi]	Breast cancer
BRCA1	NCT01482715 (completed)	A Study of Oral Rucaparib in Patients With a Solid Tumor (Phase I) or With gBRCA Mutation Ovarian Cancer (Phase II)	Rucaparib [PARPi]	Ovary, fallopian tubes, peritoneum cancers
BRCA1	NCT01434316 (active)	Veliparib and Dinaciclib in Treating Patients With Advanced Solid Tumors	Veliparib (plus Dinaciclib) [PARPi]	NSCLC (orphan drug)
BRCA1	NCT02210663 (completed)	A Phase 1 Study of Single Agent Veliparib in Japanese Subjects With Advanced Solid Tumors	Veliparib [PARPi]	NSCLC (orphan drug)
BRCA1 – CHEK2 - RAD51C – RAD54L	NCT05740956 (recruiting)	A Study of Hansoh (HS)-10502 in Patients With Advanced Solid Tumors	HS-10502 [PARPi]	
BRCA1 – CHEK2 - RAD51C – RAD54L	NCT05071209 (active)	Elimusertib for the Treatment of Relapsed or Refractory Solid Tumors	Elimusertib [ATM-kinase inhibitor]	-
BRCA1 – CHEK2 - RAD51C – RAD54L	NCT04826341	A Phase I/II Study of Sacituzumab Govitecan Plus Berzosertib in Small Cell Lung Cancer, Extra-Pulmonary Small Cell Neuroendocrine Cancer and Homologous Recombination-Deficient Cancers Resistant to PARP Inhibitors	Berzosertib [ATR-kinase inhibitor]	-

BRCA1 – CHEK2 - RAD51C – RAD54L	NCT05787587 (recruiting)	A Study of PARG Inhibitor IDE161 in Participants With Advanced Solid Tumors	IDE-161 [PARG- inhibitor]	-
BRCA1 – CHEK2 – RAD51C	NCT02873975 (completed)	A Study of LY2606368 (Prexasertib) in Patients With Solid Tumors With Replicative Stress or Homologous Repair Deficiency	Prexasertib [antiCHK1]	-
MLH1 - BRCA1	NCT02693535 (recruiting)	TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)	Nivolumab (plus ipilimumab) [anti-PD1]	Melanoma, NSCLC, renal cell carcinoma, Hodgkin lymphoma, SCCHN, urothelial cancer, mesothelioma, colorectal, oesophageal cancer
PIK3CA	NCT02260661 (completed)	Phase I, Dose Study to Look at the Safety and Pharmacokinetics of AZD8835 in Patients With Advanced Solid Tumours	AZD8835 [PIK3CA inhibitor]	-
PIK3CA	NCT05216432 (recruiting)	First-in-Human Study of Mutant-selective PI3Kα Inhibitor, RLY-2608, as a Single Agent in Advanced Solid Tumor Patients and in Combination With Fulvestrant in Patients With Advanced Breast Cancer	RLY-2608 [PIK3CA inhibitor]	-
PIK3CA	NCT03544905 (recruting)	Study to Evaluate the Safety, Tolerate, Pharmacokinetics and Preliminary Efficacy of CYH33	CYH33 [PIK3CA inhibitor]	-
PIK3CA	NCT04589845 (recruiting)	Tumor-Agnostic Precision Immuno-Oncology and Somatic Targeting Rational for You (TAPISTRY) Platform Study	GDC-0077 (Inavolisib) [PI3K inhibitor]	-
PIK3CA	NCT01306045 (active)	Molecular Profiling and Targeted Therapy for Advanced Non-Small Cell Lung Cancer, Small Cell Lung Cancer, and Thymic Malignancies	MK-2206 [AKT inibitor]	-
PIK3CA	NCT03297606 (recruting)	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR) (CAPTUR)	Temsirolimus [mTOR inhibitor]	Renal cell carcinoma, mantle cell lymphoma
PIK3CA	NCT03065062 (recruiting)	Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors	Gedatolisib (plus palbociclib) [PI3K/mTOR inhibitor]	-
PIK3CA	NCT03239015 (unknown)	Efficacy and Safety of Precision Therapy in Refractory Tumor	Everolimus [mTOR inhibitor]	Breast cancer, pancreatic

				neuroendocrine tumours, neuroendocrine tumours, advanced renal cell carcinoma, renal angiomyolipoma and tuberous sclerosis complex
PIK3CA	NCT02465060 (active)	Targeted Therapy Directed by Genetic Testing in Treating Patients With Advanced Refractory Solid Tumors, Lymphomas, or Multiple Myeloma (The MATCH Screening Trial)	Taselisib [PIK3CA inhibitor]	-
PIK3CA	NCT04591431 (active)	The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy (ROME)	Ipatasertib [AKT inibitor]	-
FGFR1	NCT03297606 (recruting)	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR) (CAPTUR)	Sunitinib [RTKs-inhibitor]	Colorectal, GIST, neuroendocrine tumours,
FGFR1	NCT01283945 (completed)	Study of Oral Lucitanib (E-3810), a Dual VEGFR-FGFR Tyrosine Kinase Inhibitor, in Patients With Solid Tumors	Lucitanib [VEGFRs/FGFR inhibitor]	-
FGFR1	NCT02693535 (recruiting)	TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)	Futibatinib [FGFR inhibitor]	Cholangiocarcinoma
FGFR1	NCT04962867 (active)	NCCH2006/MK010 Trial (FORTUNE Trial)	E7090 [FGF/FGFR inhibitor]	-
FGFR1	NCT04233567 (active)	Infigratinib for the Treatment of Advanced or Metastatic Solid Tumors in Patients With FGFR Gene Mutations	Infigratinib [FGFR inhibitor]	Cholangiocarcinoma
FGFR1	NCT01752920 (completed)	Phase 1/2 Study of Derazantinib (ARQ 087) in Adult Subjects With Advanced Solid Tumors With FGFR Genetic Alterations	Derazantinib [FGFR inhibitor]	-
FGFR1	NCT01948297 (terminated)	Debio 1347-101 Phase I Trial in Advanced Solid Tumours With Fibroblast Growth Factor Receptor (FGFR) Alterations	Debio1347 (zoligratinib) [FGFR inhibitor]	-

FGFR1	NCT04116541 (recruiting)	A Study Evaluating the Activity of Anti-cancer Treatments Targeting Tumor Molecular Alterations/Characteristics in Advanced / Metastatic Tumors. (MegaMOST)	Regorafenib [TK-inhibitor]	Colorectal cancer; GIST
FGFR1	NCT02465060 (active)	Targeted Therapy Directed by Genetic Testing in Treating Patients With Advanced Refractory Solid Tumors, Lymphomas, or Multiple Myeloma (The MATCH Screening Trial)	Erdafitinib [FGFR inhibitor]	-
FGFR1	NCT04591431 (active)	The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy (ROME)	Pemigatinib [FGFR inhibitor]	-
MYC	NCT03568656 (recruiting)	Study to Evaluate CCS1477 in Advanced Tumours	CCS1477 [p300/CBP bromodomain inhibitor]	-
MYC	NCT02873975 (completed)	A Study of LY2606368 (Prexasertib) in Patients With Solid Tumors With Replicative Stress or Homologous Repair Deficiency	Prexasertib [antiCHK1]	-
MYC	NCT02635672 (active)	Phase I Dose Escalation Study for VIP152 in Patients With Advanced Cancer	VIP152 [PTEF-b/CDK9 inhibitor]	-
MYC	NCT05159518 (completed)	A Study of PRT2527 in Participants With Advanced Solid Tumors	PRT2527 [PTEF-b/CDK9 inhibitor]	-
MYC	NCT04872166 (recruiting)	A Study of BTX-A51 in People With Advanced Solid Tumor or Non-Hodgkin Lymphoma	BTX-A51 [CK1alpha/CDK7/CDK9 inhibitor]	-
MYC	NCT02656849 (withdrawn)	BAY 1000394 for MCL-1-, MYC-, and CCNE1-Amplified Tumors	Roniciclib [panCDK inhibitor]	-
MYC	NCT04983810 (recruiting)	A Study to Investigate Fadraciclib (CYC065), in Subjects With Advanced Solid Tumors and Lymphoma	Fadraciclib [CDK2/5/9 inhibitor]	-
MYC	NCT03568656 (recruiting)	Study to Evaluate CCS1477 in Advanced Tumours	CCS1477 [p300/CBP bromodomain inhibitor]	-
MYC	NCT02873975 (completed)	A Study of LY2606368 (Prexasertib) in Patients With Solid Tumors With Replicative Stress or Homologous Repair Deficiency	Prexasertib [antiCHK1]	-
MYC	NCT02635672 (active)	Phase I Dose Escalation Study for VIP152 in Patients With Advanced Cancer	VIP152 [PTEF-b/CDK9 inhibitor]	-