Supplementary Information

Supplement to: Causer A., Tan X., Lu X. *et al. Deep spatial-omics analysis of Head & Neck carcinomas provides alternative therapeutic targets and rationale for treatment failure*

Supplementary Information Table of Contents

1. Supplementary Table 1

AKOYA Antibody	AKOYA Tag number	AKOYA PIN	Target cell
CD20	BX007	4450018	B and T cell subsets
PanCK	BX019	4450020	Epithelial cells
CD8a	BX026	4250012	T cell subsets, NK subset
Ki67	BX047	4250019	Proliferating cells
CD45Ro	BX017	4250023	Activated and memory T cells, B cell subsets
CD3e	BX045	4450030	T cells, NK-T cells, thymocytes
CD107a	BX006	4350001	Degranulation marker
HLA-DR	BX033	4450029	Activated B cells, antigen presenting cells
CD4	BX003	4350018	T cell subsets, monocytes, macrophages
CD68	BX015	4350019	Monocytes, macrophages
CD45	CX021	4450042	Hematopoietic cells
PD-1	RX046	4550038	Activation/exhaustion
PD-L1	BX043	4550072	Inhibitory signal

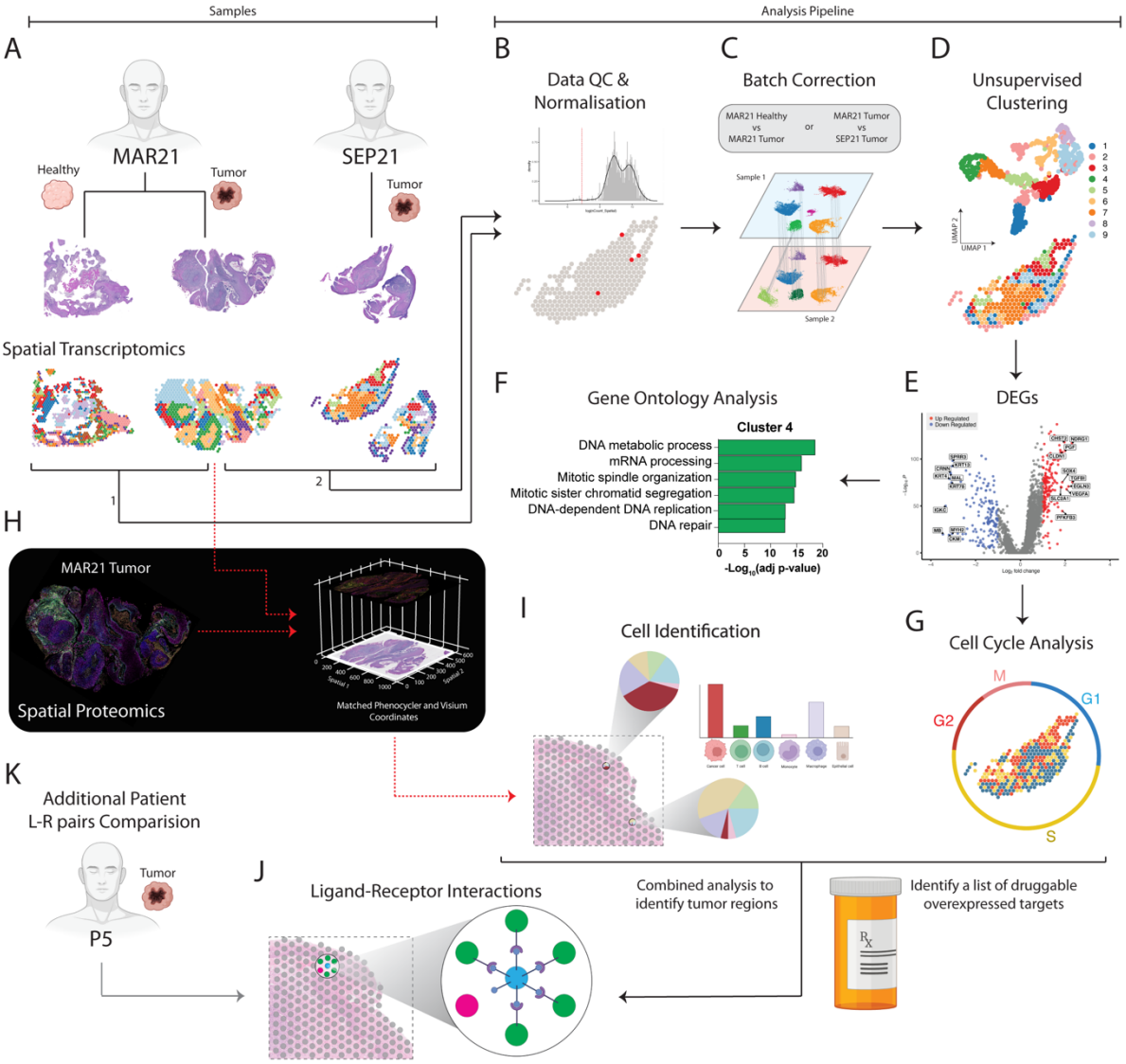
Supplementary table 1. **Spatial proteomics: PhenoCycler antibody panel.**

2. Supplementary Table 2

Cell Type	Marker Proteins
Tumor	PANCK
Tumor infiltrating cell	CD45
Dividing Tumor	PANCK, Ki67
Antigen presenting cell	CD45, HLA-DR
T cell	CD45, Cd3ε
B cell	CD45, CD20
Activated B cell	CD45, CD20, CD8
CD8 T cell	CD45, Cd3ε, CD8
CD4 T cell	CD45, Cd3ε, CD4
Activated CD8 T cell	CD45, Cd3ε, CD8, CD107a
Activated CD4 T cell	CD45, Cd3ε, CD4, CD107a
Memory CD8 T cell	CD45, Cd3ε, CD8, CD45R0
Memory CD4 T cell	CD45, Cd3ε, CD4, CD45R0
Dividing CD8 T cell	CD45, Cd3ε, CD8, Ki67
Dividing CD4 T cell	CD45, Cd3ε, CD4, Ki67
Macrophage/Monocyte	CD45, CD68
Dividing Macrophage	CD45, CD68, Ki67

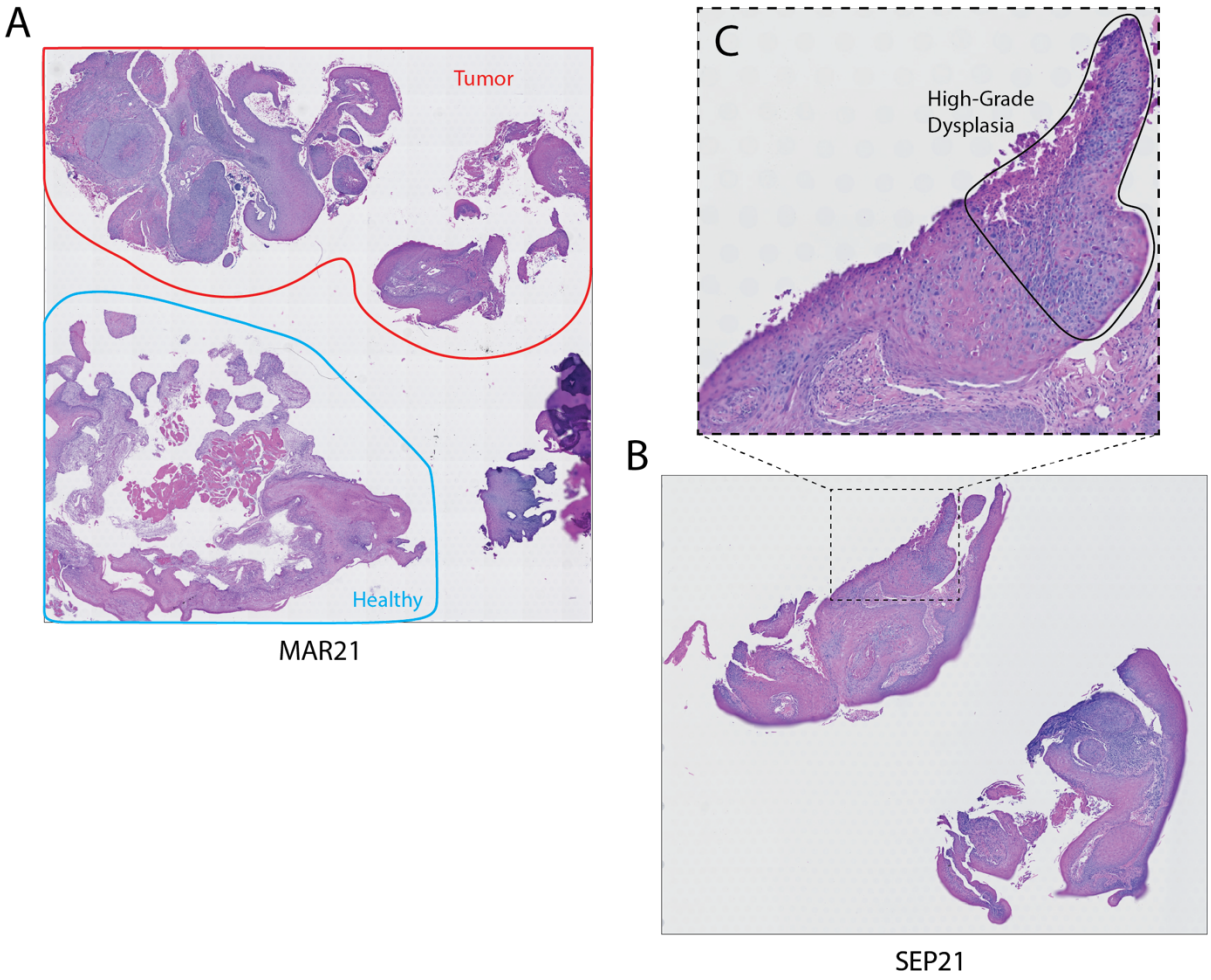
Supplementary table 2. **Spatial proteomics: cell type annotation based on surface protein expression.**

3. Supplementary Figure 1



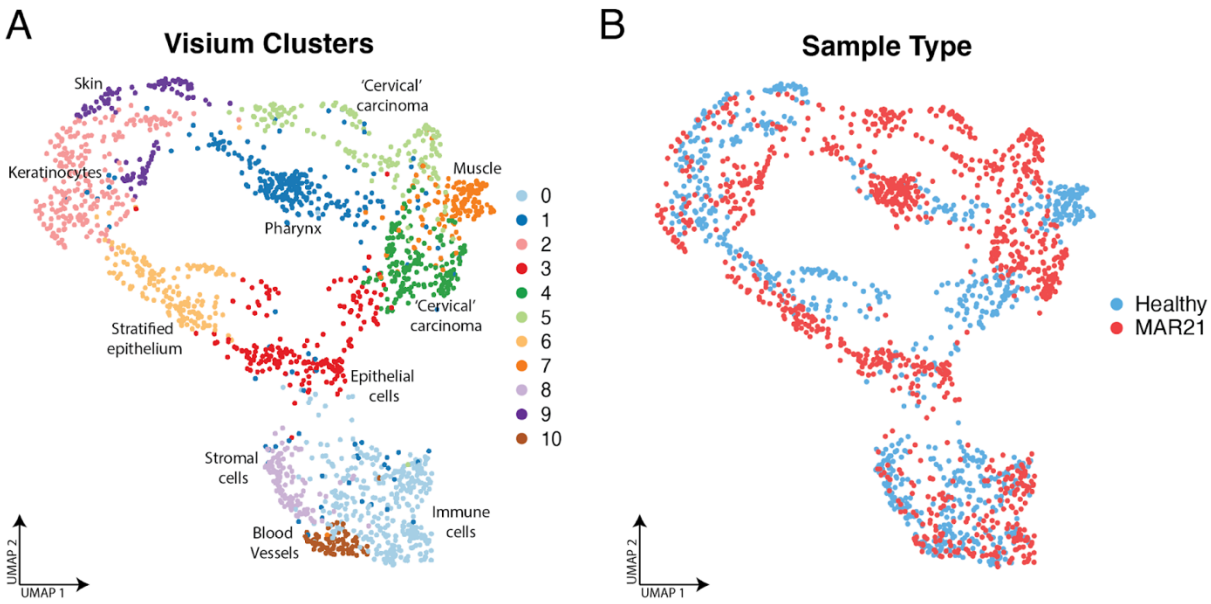
Supplementary Figure 1. **Flow-diagram representing the implemented workflow. A.** Displays the different samples being analyzed within the study. Two comparisons are performed: 1) between healthy and tumor samples of MAR21 sample. 2) between MAR21 and SEP21 tumor samples. Both comparisons undergo analysis through the same pipeline which includes: **B.** Data quality control and normalization, **C.** Batch correction between samples, **D.** Unsupervised clustering to identify spots of similar transcriptomic profiles. **E.** Differential gene expression analysis, **F.** Gene ontology term enrichment analysis, and **G.** Cell cycle state analysis. **H.** In addition to spatial transcriptomics, spatial proteomics was performed on the MAR21 tumor sample. Integration of spatial transcriptomics and proteomics was performed to inform **I.** Spot cell composition. The overall analysis was used to identify and analyze the tumor regions within the samples. **J.** Ligand-receptor (L-R) interaction analysis was then performed to identify the most active L-R pairs which are druggable targets. **K.** An additional patient was analyzed in combination to assess if the L-R pairs are patient-specific. **L.** L-R pair activity was further assessed through pathway analysis of differentially expressed genes. **M.** The collective findings were then used to determine the top druggable targets specific to the patient.

4. Supplementary Figure 2



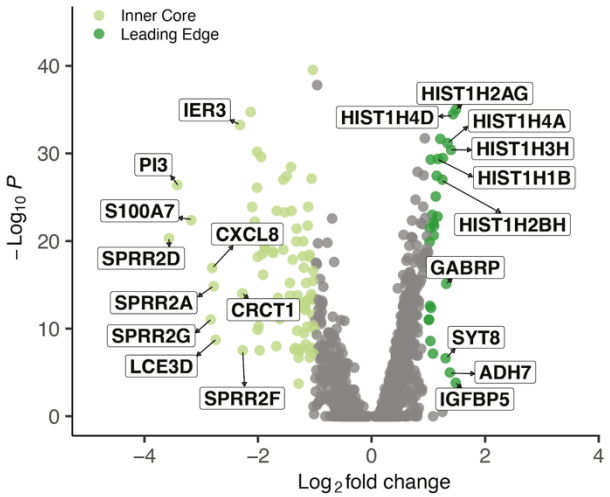
Supplementary Figure 2. **High-resolution H&E images of MAR21 and SEP21 samples. A.** Displays the high-resolution H&E image of both the healthy and tumor MAR21 sample. **B.** The high-resolution H&E image of SEP21 tumor samples. C. The highlighted box represents the tissue region which pathologists identified as high-grade dysplasia after re-analysis of the original H&E image. The raw images have been made publicly accessible at https://doi.org/10.48610/698bb9e.

5. Supplementary Figure 3



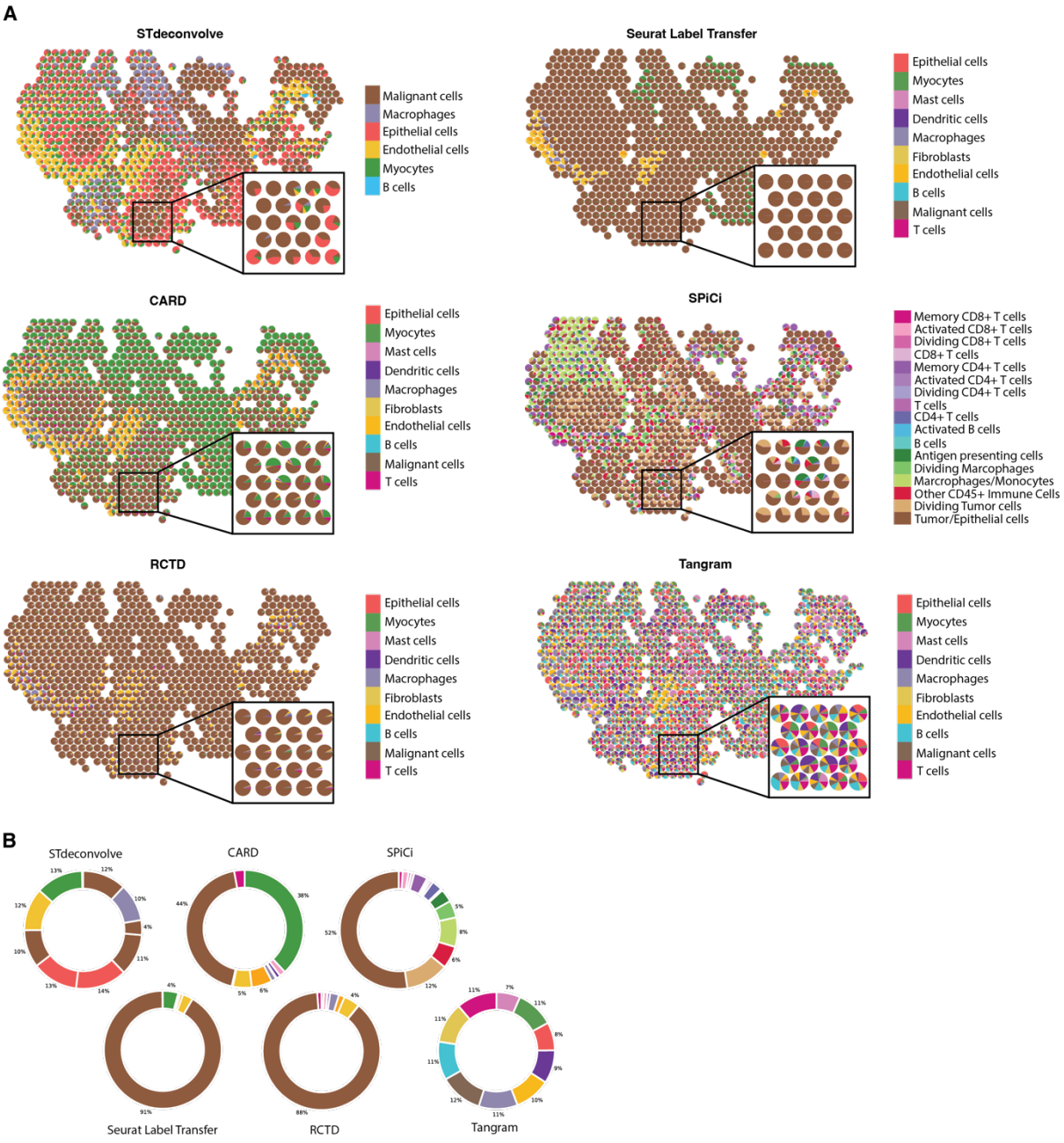
Supplementary Figure 3. **UMAP representation of unbiased Visium clustering of MAR21 and healthy paired samples**. UMAP of clusters highlights distinction and separation between populations. **A.** Cluster annotations were generated by comparing differentially overexpressed genes with a reference database (JENSENs Tissues; EnrichR). **B.** Sample type UMAP displays batch correction between healthy (blue) and MAR21 OPSCC (red) samples.

6. Supplementary Figure 4



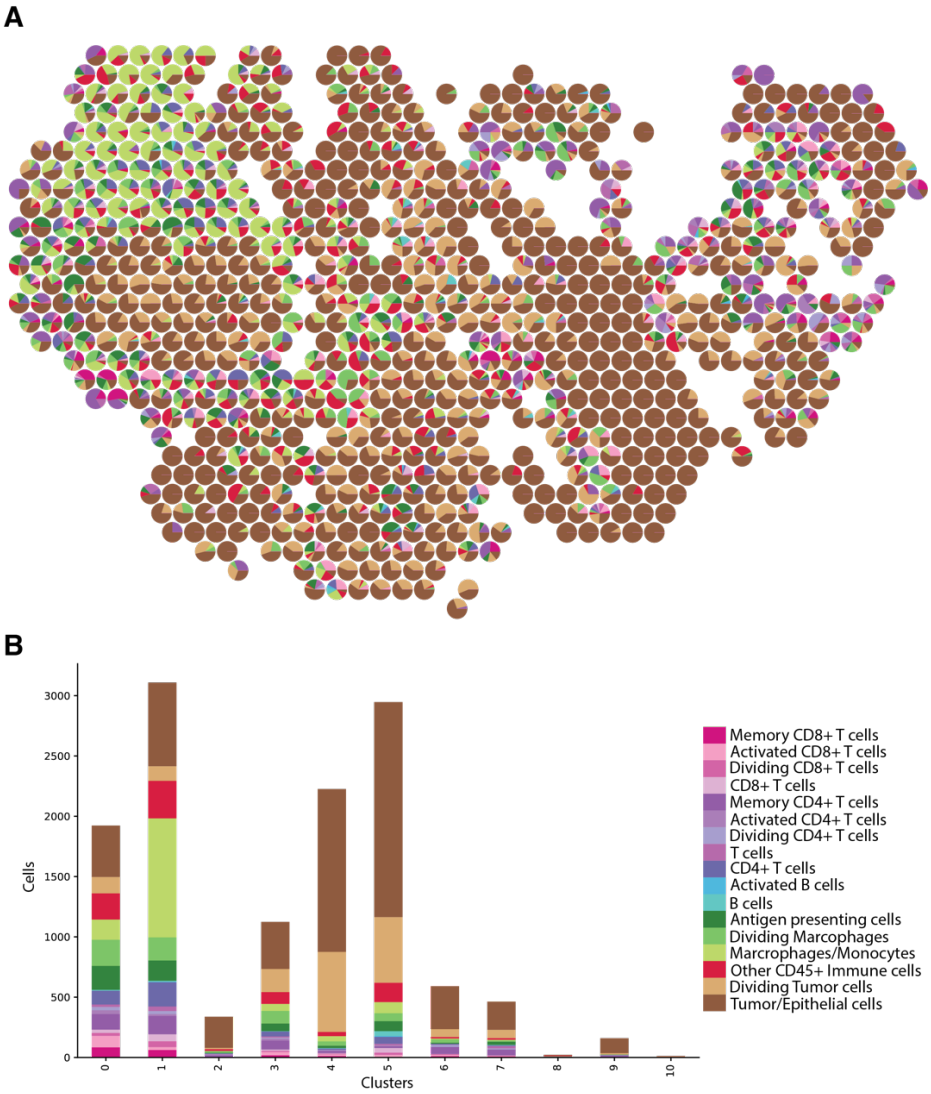
Supplementary Figure 4. **Distinct transcriptional profiles of inner core and leading-edge clusters.** DEGs between newly defined Visium clusters 4 (dark green) and 5 (light green). Significant DEGs with Wilcoxon test p-value < 0.001 and fold-change >1 are colored based on cluster.

7. Supplementary Figure 5



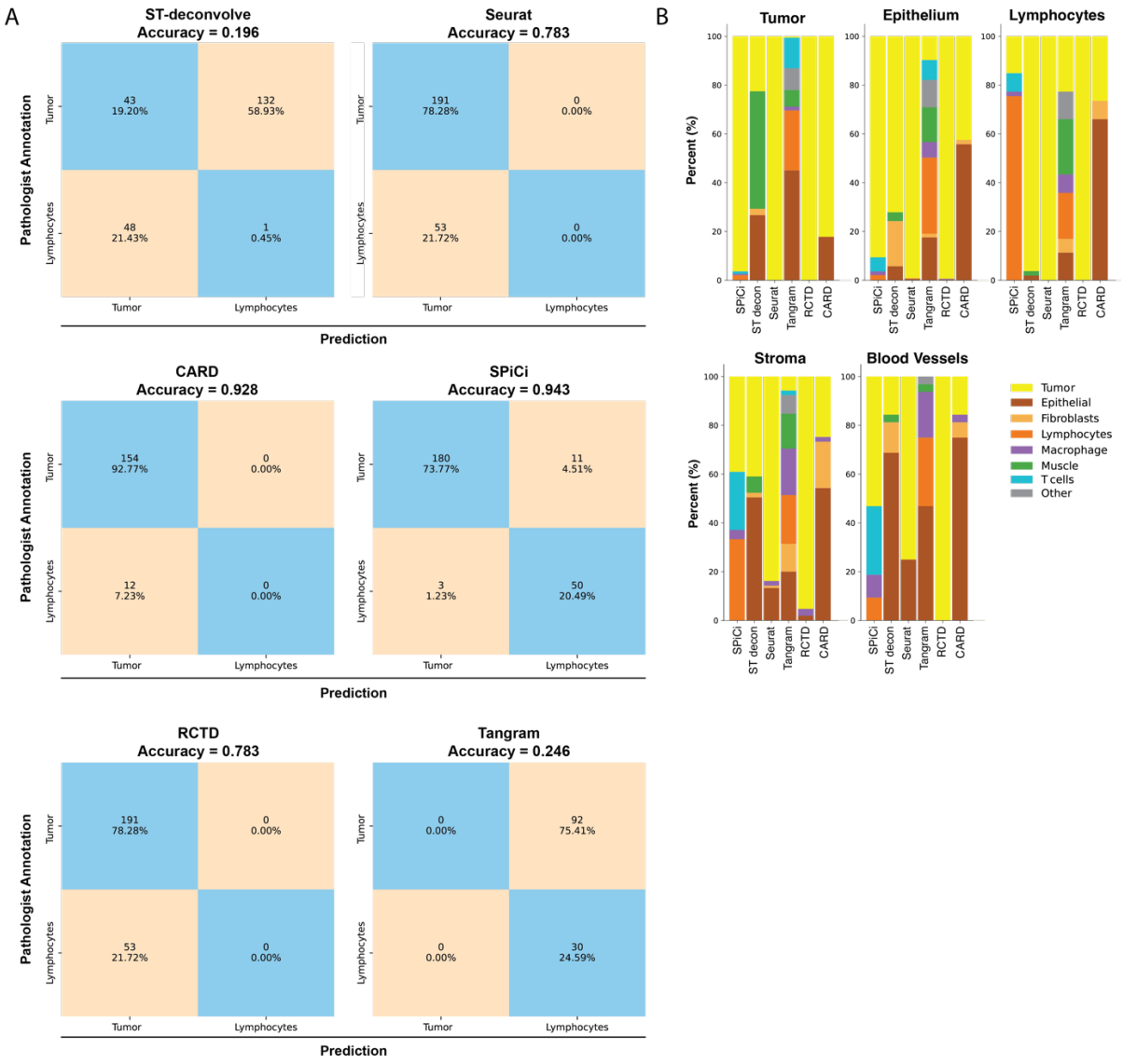
Supplementary Figure 5. **Spatial transcriptomics (Phenocycler)-informed cell identification (*SPiCi*) and established transcription-based deconvolution methods. A.** Displays spot cell annotation of tumor sample using each algorithm. Spots are represented as pie graphs denoting the proportions of each cell type identified within each spot capture region. Enlarged regions encapsulate the outer proliferating ring of the tumor and the immune cell infiltrated core. **B.** Overall percentages of different cell types identified by each approach (across all spots combined).

8. Supplementary Figure 6



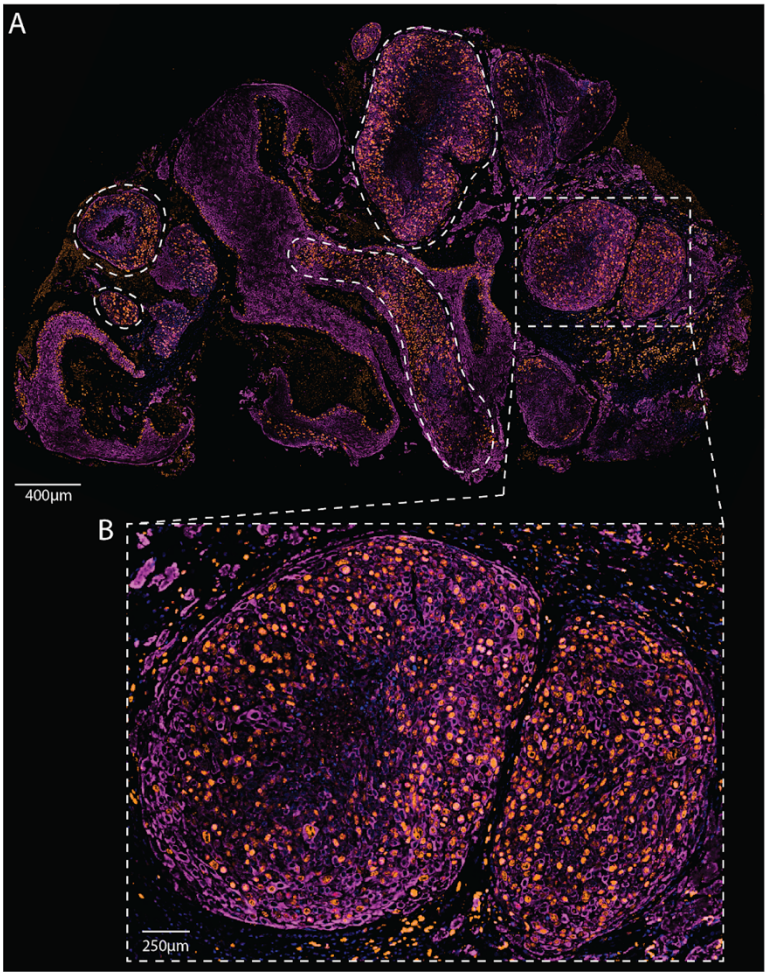
Supplementary Figure 6. **Integrated Spatial-Omic characterization of tumor immune cell microenvironments. A.** Visium spot cell identification of MAR21 OPSCC using *SPiCi*. Spots are presented as pie-charts representing the relative proportions of cell types located within each spot. **B.** Quantification of cell-types found within each Visium cluster.

9. Supplementary Figure 7



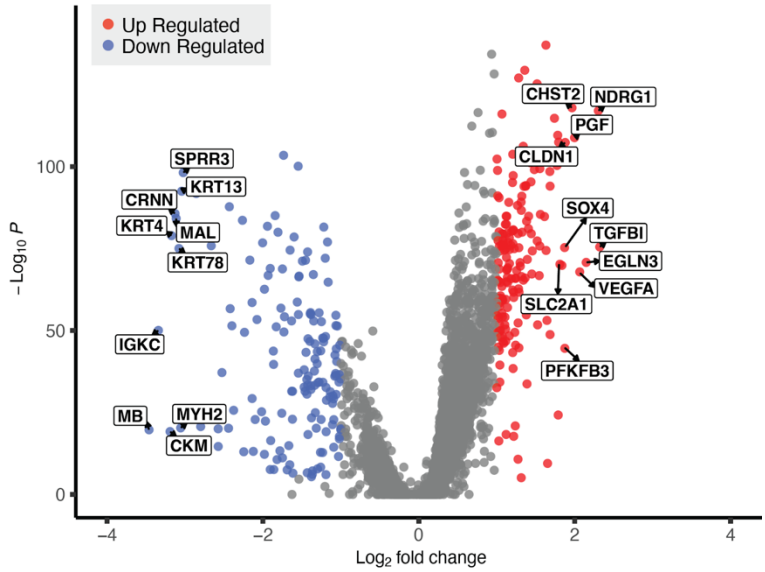
Supplementary Figure 7. **Comparison of deconvolution methods and *SPiCi* results with pathologist annotation. A.** Confusion matrices were calculated to evaluate the performance of each method at detecting tumor and lymphocyte cells compared to the ground truth pathological annotation. The cell type label for each spot is determined by the cell type with the highest proportion (i.e., classification probability) for that spot, calculated by each method. The inferred spot labels were then compared with the ground truth pathological annotations. Accuracy rates were calculated based on results generated from each confusion matrix. **B.** Bar graphs indicate the proportion of various cell types predicted by each method with respect to each cell type identified by pathological annotation.

10. Supplementary Figure 8



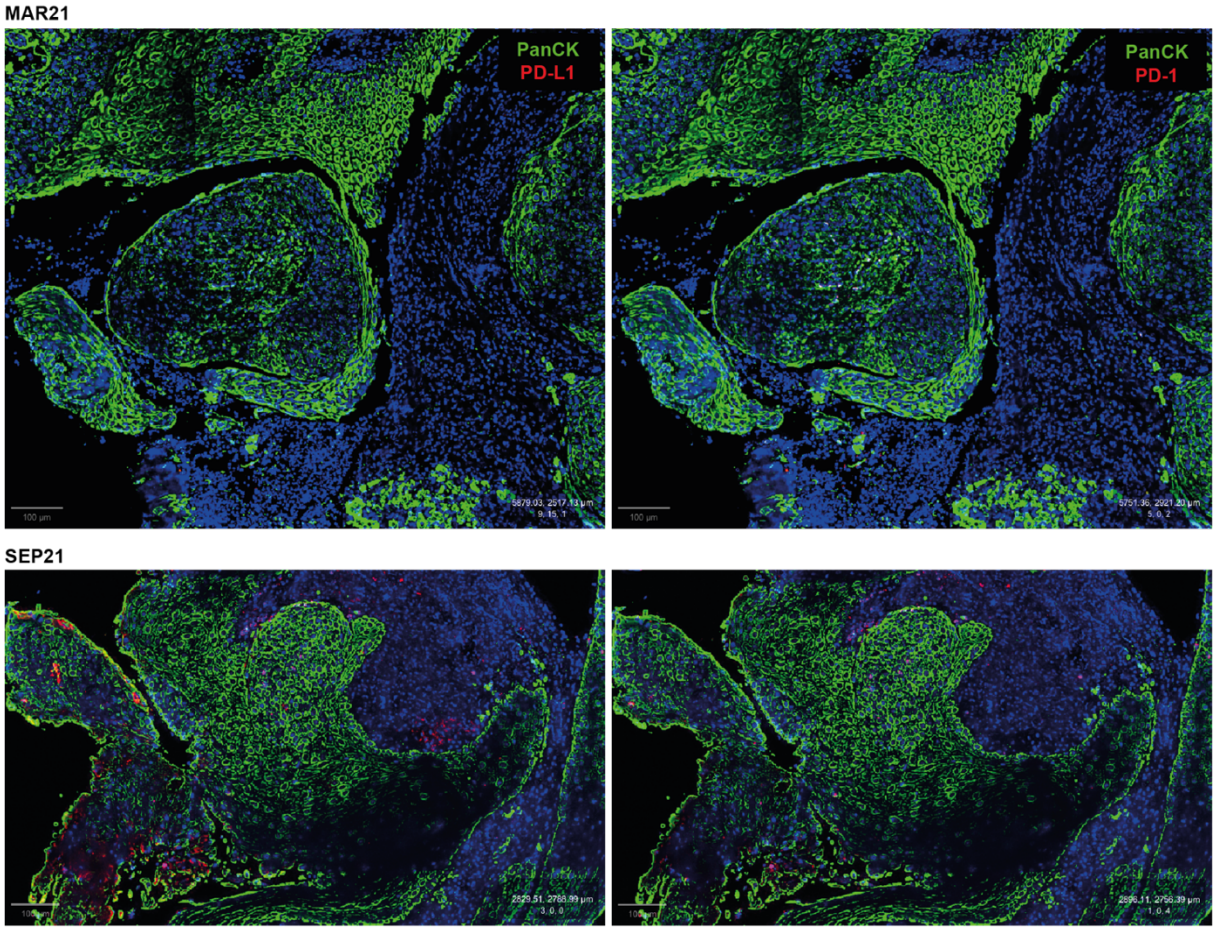
Supplementary Figure 8. **Localization of proliferating tumor cells. A.** PhenoCycler fluorescence images displaying PanCK+ (Purple) and Ki67+ (Orange) cells across the MAR21 OPSCC sample. **B.** Tumor region of interest presents with leading edge of active proliferating cells and inactive tumor core.

11. Supplementary Figure 9



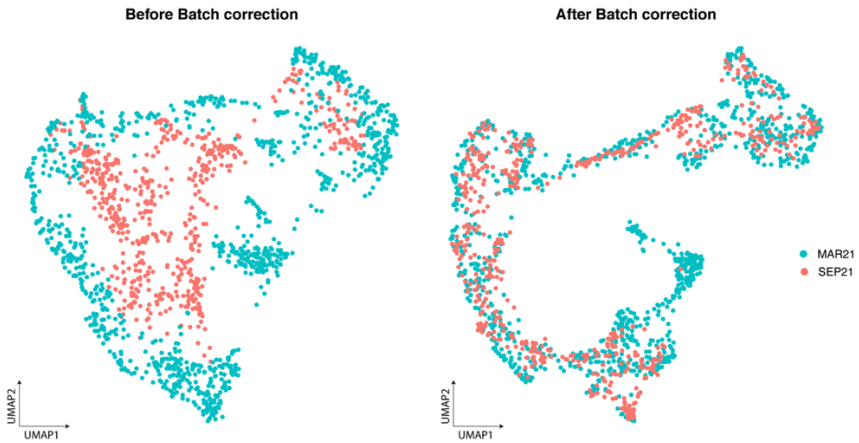
Supplementary Figure 9. **Differential analysis of transcriptional profiles of tumor clusters within MAR21 OPSCC.** DEGs of the combined tumor clusters relative to all other clusters. Significantly up-regulated and down-regulated genes are highlighted in red and blue respectively (Wilcoxon test p-value < 0.001 and an absolute fold- change > 1). The top 10 over- and under-expressed genes are annotated.

12. Supplementary Figure 10



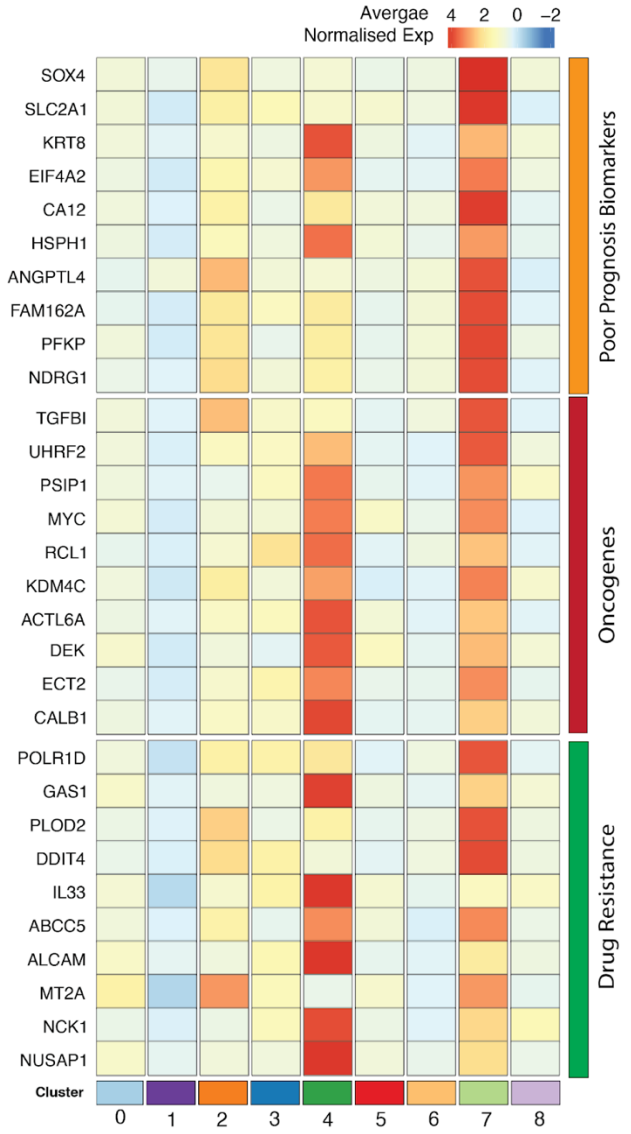
Supplementary Figure 10. **PD-L1 and PD-1 protein staining. A.** PHENOCYCLER fluorescence images displaying PanCK+ (green) and PD-L1 (red, *left*) or PD-1 (red, *right*) cells across the MAR21 and SEP21 OPSCC samples.

13. Supplementary Figure 11



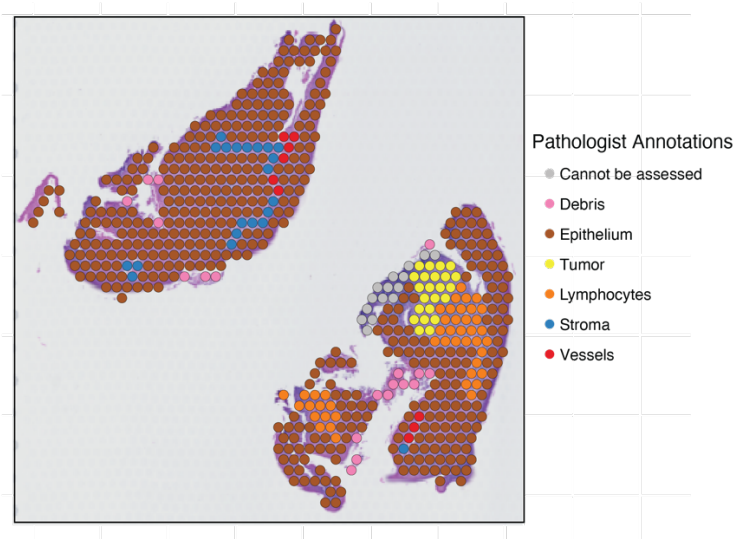
Supplementary Figure 11. **Visium data integration and batch correction of tumor tissues.** Spatial transcriptomic data generated from MAR21 and SEP21 tumors was integrated (*left)* and batch effect corrected (*right*) using the Seurat anchor integration pipeline.

14. Supplementary Figure 12



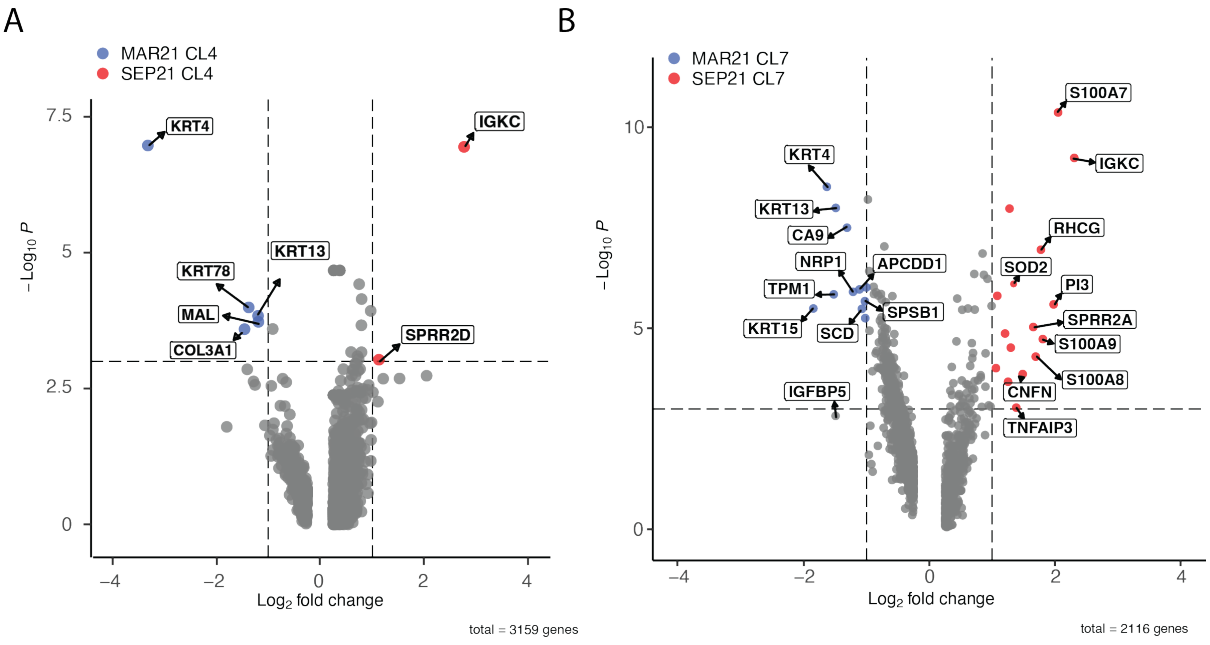
Supplementary Figure 12. **Tumor transcriptional profile recapitulated in recurrent SEP21 OPSCC.** Relative expression of poor prognosis markers (red), oncogenes (orange) and drug resistance genes (green), previously identified from the combined tumor cluster within MAR21, across each newly defined cluster generated through comparing OPSCC samples. The top 9 genes of each category were displayed. Colors gradient represents average normalized expression values across all spots in each cluster, which were z-transformed by genes (rows of the heatmap).

15. Supplementary Figure 13



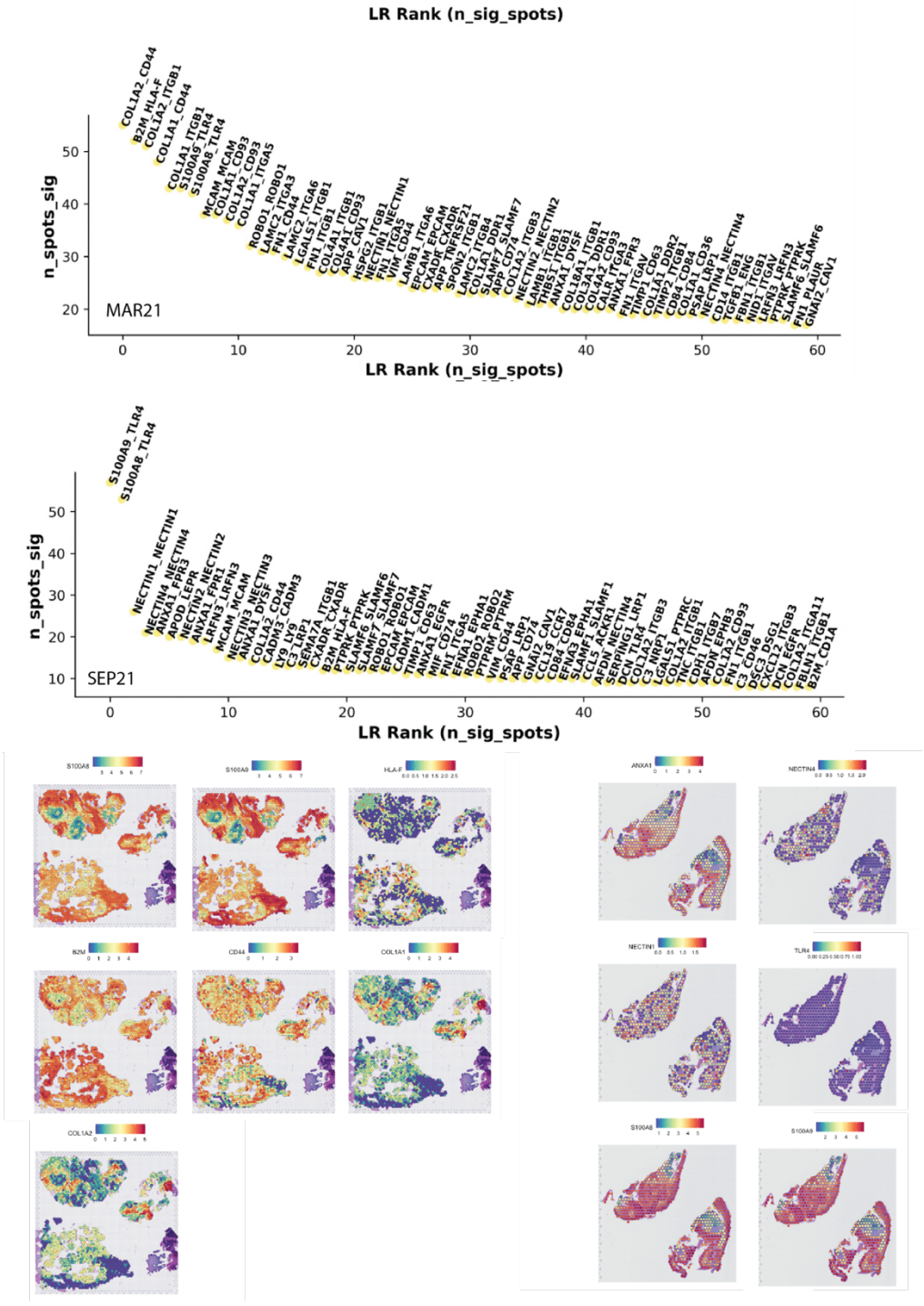
Supplementary Figure 13. **Initial Pathologist annotation of SEP21 OPSCC sample.** Colored spots identify different morphological tissue structure identified from the H&E image by a clinical pathologist.

16. Supplementary Figure 14



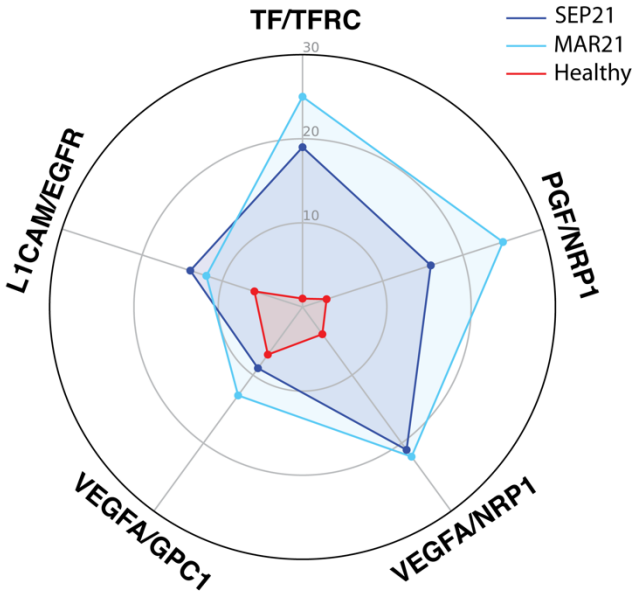
Supplementary Figure 14. **Differential expression analysis of tumor clusters 4 and 7 in the MAR21-SEP21 OPSCC integrated dataset.** DEGs of the tumor clusters CL4 (A) and CL7 (B) from MAR21 and SEP21 samples. Significantly up-regulated and down-regulated genes are highlighted in red and blue respectively (Wilcoxon test p-value < 0.001 and an absolute fold-change > 1). The top over- and under-expressed genes based on fold change and P-values are annotated.

17. Supplementary Figure 15



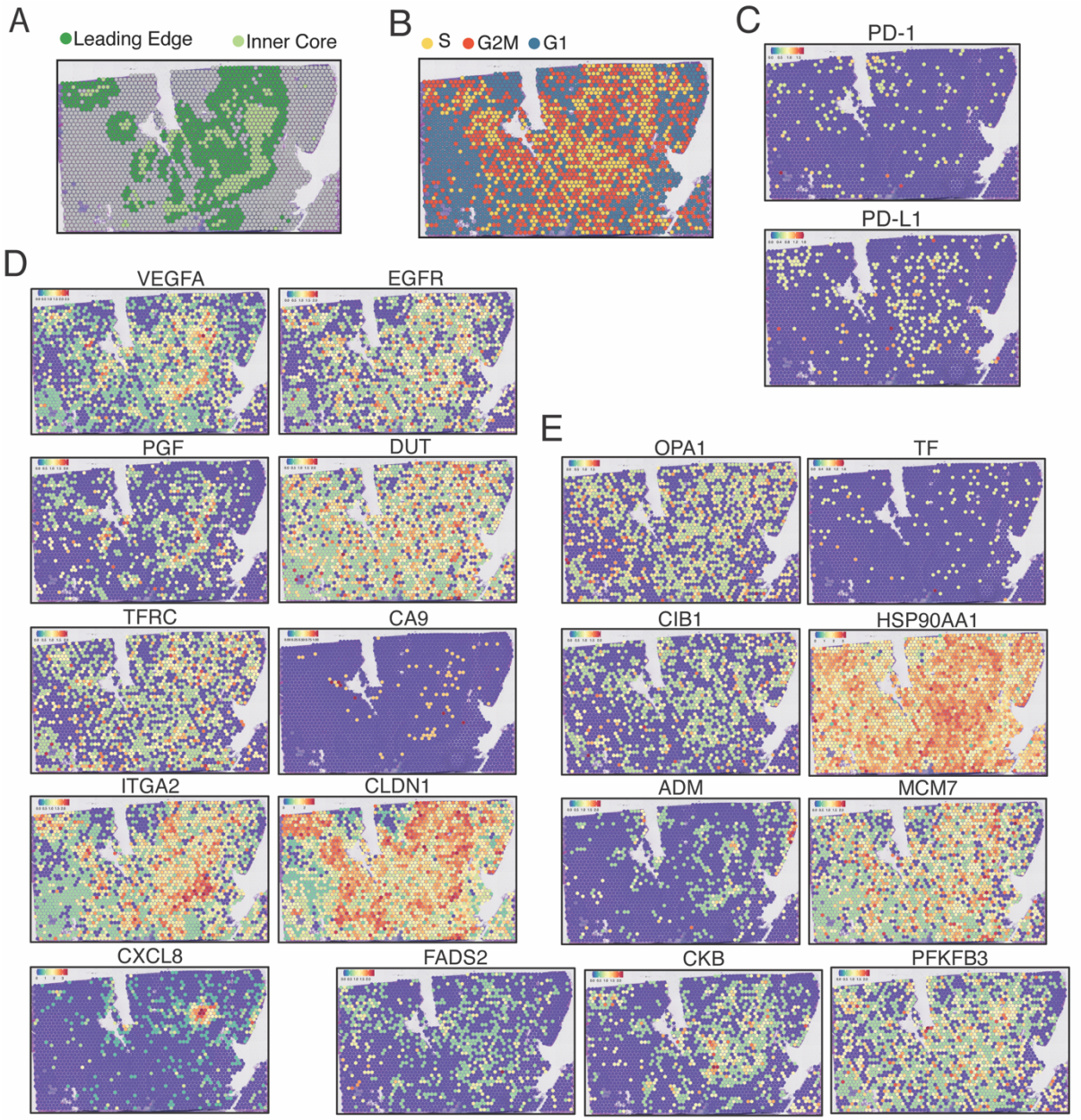
Supplementary Figure 15. **Ligand-receptor interaction analysis in MAR21 and SEP21 tissues. A.** Ranking of top 60 Ligand/Receptor (L/R) expressed by the MAR21 (*top*) and recurrent SEP21 (bottom). Rank was based on the number of spots with significant interactions of each L/R pair across each sample. **B.** Spatial expression of top L/R pairs expressed by MAR21(*left*) and SEP21(*right*). In all feature plots, the relative gene expression per spot is indicated by the coloured scale bars.

18. Supplementary Figure 16



Supplementary Figure 16. **Transcriptional comparison between MAR21 and recurrent SEP21 and ligand-receptor interaction analysis for therapeutic target selection.** Spider-plot represents the top 5 most active L-R pairs found across tumor tissue based on the number of spots with significant interactions using the L-R pairs. Red line, healthy tissue; dark blue, SEP21; light blue, MAR21.

19. Supplementary Figure 17



Supplementary Figure 17. **Top druggable targets differ between additional OPSCC patients. A.** Spatial representation of Visium clusters identified as tumor leading edge (dark green) and inner core (light green) within an additional OPSCC patient. **B.** Cell cycle phase of each spot based on relative expression of specific cell phase genes. **C.** Spatial expression of genes targeted by Nivolumab and Pembrolizumab targeted *PD-1/PD-L1* pathway. **D.** Spatial visualization of gene expression of genes targeted by previously identified clinical therapies. **E.** Spatial localization of gene expression levels for select experimental drug therapies. In all feature plots, the relative gene expression per spot is indicated by the coloured scale bars.

Supplementary table 3. **Gene classification based on function reported in the literature in the cancer setting.**

Gene	Categories	Ref
HAUS6	Oncogenes	[1]
DBN1	Oncogenes	[2-4]
CCNL1	Oncogenes	[5]
ACTL6A	Oncogenes	[6]
CHAF1A	Oncogenes	[7,8]
DEK	Oncogenes	[9]
ECT2	Oncogenes	[10,11]
EIF4EBP1	Oncogenes	[12]
FXR1	Oncogenes	[13]
JUN	Oncogenes	[14]
KDM4C	Oncogenes	[15]
MYBL2	Oncogenes	[16]
MYC	Oncogenes	[17]
NSD2	Oncogenes	[18]
PFDN2	Oncogenes	[19]
PSIP1	Oncogenes	[20]
RNF19A	Oncogenes	[21]
TAGLN2	Oncogenes	[22,23]
TGFBI	Oncogenes	[24]
UHRF2	Oncogenes	[25]
VAV3	Oncogenes	[26,27]
JAG1	Oncogenes	[28,29]
CENPW	Oncogenes	[30,31]
SMC4	Good and Poor prognosis biomarker	[32,33]
COL7A1	Good prognosis biomarker	[34]

CXADR	Good prognosis biomarker	[35]
FOXRED2	Good prognosis biomarker	[36]
LPAR3	Good prognosis biomarker	[37]
MEI1	Good prognosis biomarker	[38]
NEFH	Good prognosis biomarker	[39]
VLDLR	Good prognosis biomarker	[40]
PGK1	Poor prognosis biomarker	[41]
ANGPTL4	Poor prognosis biomarker	[42]
ANP32E	Poor prognosis biomarker	[43]
ATP13A3	Poor prognosis biomarker	[44]
BHLHE40	Poor prognosis biomarker	[45,46]
CA12	Poor prognosis biomarker	[47]
CALB1	Poor prognosis biomarker	[48]
CCT3	Poor prognosis biomarker	[49-51]
CENPJ	Poor prognosis biomarker	[52]
CPA4	Poor prognosis biomarker	[53]
CSE1L	Poor prognosis biomarker	[54]
DSC3	Poor prognosis biomarker	[55]
DVL3	Poor prognosis biomarker	[56]
EIF4A2	Poor prognosis biomarker	[57]
FAM162A	Poor prognosis biomarker	[58]
FAT2	Poor prognosis biomarker	[59]
GTF3A	Poor prognosis biomarker	[60]
HILPDA	Poor prognosis biomarker	[61]
HSPA1A	Poor prognosis biomarker	[62]
HSPA1B	Poor prognosis biomarker	[62]
HSPE1	Poor prognosis biomarker	[63]

HSPH1	Poor prognosis biomarker	[64]
IER3	Poor prognosis biomarker	[65]
KRT8	Poor prognosis biomarker	[66]
LAMA5	Poor prognosis biomarker	[67,68]
LPCAT1	Poor prognosis biomarker	[69,70]
NFIL3	Poor prognosis biomarker	[71]
NRARP	Poor prognosis biomarker	[72,73]
NUP58	Poor prognosis biomarker	[74]
NXPH4	Poor prognosis biomarker	[75]
PCLAF	Poor prognosis biomarker	[76]
PFKP	Poor prognosis biomarker	[77]
PLAUR	Poor prognosis biomarker	[78]
PLPP2	Poor prognosis biomarker	[79]
PNCK	Poor prognosis biomarker	[80]
PODXL2	Poor prognosis biomarker	[81]
PSMD2	Poor prognosis biomarker	[82]
PTHLH	Poor prognosis biomarker	[83]
PUM3	Poor prognosis biomarker	[84]
RFC3	Poor prognosis biomarker	[85]
RFC4	Poor prognosis biomarker	[86]
RHOV	Poor prognosis biomarker	[21]
RUVBL1	Poor prognosis biomarker	[87]
SAT1	Poor prognosis biomarker	[88]
SLC2A1	Poor prognosis biomarker	[89]
SNAI2	Poor prognosis biomarker	[90]
SOD2	Poor prognosis biomarker	[91,92]
SOX4	Poor prognosis biomarker	[93]

STC2	Poor prognosis biomarker	[94,95]
TBL1XR1	Poor prognosis biomarker	[96]
TCN1	Poor prognosis biomarker	[97]
TCP1	Poor prognosis biomarker	[98]
TFDP1	Poor prognosis biomarker	[99]
TMEM189	Poor prognosis biomarker	[100,101]
U2SURP	Poor prognosis biomarker	[102]
UBE2C	Poor prognosis biomarker	[26]
YEATS2	Poor prognosis biomarker	[103]
ABCC5	Drug Resistance	[104]
ALCAM	Drug Resistance	[105]
CALCRL	Drug Resistance	[106,107]
FBXO42	Drug Resistance	[108]
GAS1	Drug Resistance	[109]
IL33	Drug Resistance	[110]
MKNK2	Drug Resistance	[111]
MT2A	Drug Resistance	[112,113]
NCK1	Drug Resistance	[114]
NUSAP1	Drug Resistance	[115]
PGF	Drug Resistance	[116]
PLOD2	Drug Resistance	[117]
POLR1D	Drug Resistance	[118]
PGK1	Drug Resistance	[41]
NES	Drug Resistance	[119]
CERS2	Tumor suppressor	[120]
DLG1	Tumor suppressor	[121]
FLNB	Tumor suppressor	[122]

GADD45A	Tumor suppressor	[123]
HLTF	Tumor suppressor	[124]
HMG20B	Tumor suppressor	[125]
IL12RB2	Tumor suppressor	[126,127]
ILF3	Tumor suppressor	[128]
IRF6	Tumor suppressor	[129,130]
MT1G	Tumor suppressor	[131]
MT1X	Tumor suppressor	[132]
NDRG1	Tumor suppressor	[133]
RBM38	Tumor suppressor	[134]
RCL1	Tumor suppressor	[135]
RSRC1	Tumor suppressor	[136]
SEMA4B	Tumor suppressor	[137]
DDIT4	Tumor suppressor	[138,139]
EFNA1	Tumor suppressor	[140]
NRG1	Tumor suppressor	[141]
ALDH1A3	Drug Resistance (chemoresistance in colorectal cancer); Experimental target	[142,143]
HMGB1	Experimental target	[144]
CNFN	Good prognosis marker	[145]
CYSRT1	Good prognosis marker	[146,147]
IGKC	Good prognosis marker	[148]
IGKV4-1	Good prognosis marker	[149]
IGLC1	Good prognosis marker	[150]
JCHAIN	Good prognosis marker	[151]
IGHA1	Good prognosis marker	[152]
IGHG1	Good prognosis marker	[152]
IGHG2	Good prognosis marker	[152]

IGHG4	Good prognosis marker	[152]
CALB1	Oncogene	[48,153]
LCN2	Oncogene	[154]
TGFBI	Oncogene	[24]
XBP1	Oncogene	[155]
COL1A1	Poor prognosis marker	[156]
COL1A2	Poor prognosis marker	[157]
COL3A1	Poor prognosis marker	[158]
CRNN	Poor prognosis marker	[159]
ECM1	Poor prognosis marker	[160,161]
EMP1	Poor prognosis marker	[162]
ERO1A	Poor prognosis marker	[163]
GLUL	Poor prognosis marker	[164,165]
KLK13	Poor prognosis marker	[166]
KLK6	Poor prognosis marker	[167,168]
KLK7	Poor prognosis marker	[168]
KRT13	Poor prognosis marker	[169]
KRT4	Poor prognosis marker	[170]
KRT78	Poor prognosis marker	[171]
KRT8	Poor prognosis marker	[171]
LCE3D	Poor prognosis marker	[172,173]
NDRG1	Poor prognosis marker	[174,175]
PRSS27	Poor prognosis marker	[176]
SOD2	Poor prognosis marker	[91,92]
SPRR2A	Poor prognosis marker	[177,178]
SPRR2D	Poor prognosis marker	[178]
SPRR3	Poor prognosis marker	[179]

HOPX	Tumor suppressor	[180,181]
MAL	Tumor suppressor	[182]
SLURP1	Tumor suppressor	[183,184]
SLURP2	Tumor suppressor	[183]
SPINK5	Tumor suppressor	[185]
SPINK7	Tumor suppressor	[186]
TGM3	Tumor suppressor	[187,188]
TM4SF1	Tumor suppressor (gastric carcinoma); poor prognosis marker (epithelial cancers)	[189,190]

Supplementary table 4. **Identified clinical and preclinical targets.**

Gene	Drug name	Company name	Indication	Development Stage
CA9 [47,191]	SLC-0111	SignalChem Lifesciences Corp	Pancreatic Ductal Adenocarcinoma	Phase II
DUT [192]	TAS-114	Taiho Pharmaceutical Co Ltd	Adenocarcinoma Of The Gastroesophageal Junction; Gastric Cancer; Non-Small Cell Lung Cancer	Phase II
			Metastatic Breast Cancer; Metastatic Colorectal Cancer; Pancreatic Cancer	Phase I
EGFR [193]	futuximab + modotuximab	Symphogen A/S	Metastatic Colorectal Cancer	Phase III
	abivertinib maleate	Sorrento Therapeutics Inc	Metastatic Hormone Refractory (Castration Resistant, Androgen-Independent) Prostate Cancer; Burkitt Lymphoma; Diffuse Large B-Cell Lymphoma; Follicular Lymphoma; Mantle Cell Lymphoma; Marginal Zone B-cell Lymphoma; Refractory Chronic Lymphocytic Leukemia (CLL); Relapsed Chronic Lymphocytic Leukemia (CLL); Waldenstrom Macroglobulinemia (Lymphoplasmacytic Lymphoma)	Phase I
	abivertinib maleate	Sorrento Therapeutics Inc	Hairy Cell Leukemia; Non-Small Cell Lung Cancer; Prostate Cancer	Phase II

	abivertinib maleate	Sorrento Therapeutics Inc	Non-Small Cell Lung Cancer	Phase III
	afatinib dimaleate	More than 10 companies	Non-Small Cell Lung Cancer; Squamous Non-Small Cell Lung Cancer	Marketed
		Boehringer Ingelheim International GmbH	Anaplastic Astrocytoma; Anaplastic Oligoastrocytoma; Chordoma; Leptomeningeal Disease (Neoplastic Meningitis, Leptomeningeal Carcinomatosis); Low-Grade Glioma; Medulloblastoma; Meningioma; Oligodendroglioma; Pituitary Tumor; Recurrent Glioblastoma Multiforme (GBM)	Phase I
			Chordoma; Esophageal Cancer; Gastric Cancer; Metastatic Transitional (Urothelial) Tract Cancer; Squamous Cell Carcinoma; Uterine Cancer; Lymphoma; Refractory Multiple Myeloma	Phase II
	alflutinib mesylate	Allist Shanghai Pharmaceutical Technology Co Ltd	Non-Small Cell Lung Cancer	Marketed
			Lung Adenocarcinoma	Phase I
		Arrivent Biopharma Inc	Non-Small Cell Lung Cancer	Phase II
	amelimumab	Shanghai Sailun Biotechnology Co Ltd	Colorectal Cancer	Phase II
		Janssen Inc	Non-Small Cell Lung Cancer	Marketed
		Janssen-Cilag Pharma GmbH	Non-Small Cell Lung Cancer	Marketed

		Johnson & Johnson	Breast Cancer; Colorectal Cancer; Gastroesophageal (GE) Junction Carcinomas; Head and Neck Cancer Squamous Cell Carcinoma; Hepatocellular Carcinoma; Kidney Cancer (Renal Cell Cancer); Malignant Mesothelioma; Medullary Thyroid Cancer; Non-Small Cell Lung Cancer; Ovarian Cancer; Solid Tumor	Phase I
			Esophageal Cancer; Gastric Cancer; Gastroesophageal (GE) Junction Carcinomas; Metastatic Colorectal Cancer	Phase II
			Non-Small Cell Lung Cancer	Phase III
	AMX-3009	Arromax Pharmatech Co Ltd	Solid Tumor	Phase I
	ASK-120067	Jiangsu Aosaikang Pharmaceutical Co Ltd	Non-Small Cell Lung Cancer	Phase III
	aumolertinib mesylate	Jiangsu Hansoh Pharmaceutical Group Co Ltd	Non-Small Cell Lung Cancer	Marketed
		EQRx Inc	Non-Small Cell Lung Cancer	Phase III
		Jiangsu Hansoh Pharmaceutical Group Co Ltd	Non-Small Cell Lung Cancer	Phase III
	BAY-2927088	Bayer AG	Non-Small Cell Lung Cancer	Phase I

	BBT-176	Bridge Biotherapeutics Inc	Non-Small Cell Lung Cancer	Phase II
	BC-001	Dragonboat Biopharmaceutical (Shanghai) Co Ltd	Unspecified Cancer	Phase III
	BCA-101	Bicara Therapeutics Inc	Anal Cancer; Anaplastic Thyroid Cancer; Colorectal Cancer; Epithelial Ovarian Cancer; Gastric Cancer; Glioblastoma Multiforme (GBM); Head and Neck Cancer Squamous Cell Carcinoma; Hepatocellular Carcinoma; Lung Cancer; Pancreatic Cancer; Solid Tumor; Squamous Cell Carcinoma	Phase II
	BDTX-1535	Black Diamond Therapeutics Inc	Glioblastoma Multiforme (GBM); Non-Small Cell Lung Cancer	Phase I
	BEBT-109	Guangzhou BeBetter Medicine Technology Co Ltd	Non-Small Cell Lung Cancer	Phase II
	befortinib mesylate	InventisBio Co Ltd	Non-Small Cell Lung Cancer	Phase III
	BLU-451	Blueprint Medicines Corp	Non-Small Cell Lung Cancer	Phase II
	BLU-701	Zai Lab Ltd	Non-Small Cell Lung Cancer	Phase II
	BLU-945	Blueprint Medicines Corp	Non-Small Cell Lung Cancer	Phase II

	BPI-361175	Betta Pharmaceuticals Co Ltd	Non-Small Cell Lung Cancer; Solid Tumor	Phase II
	BPI-7711	Beta Pharma Inc	Non-Small Cell Lung Cancer	Phase II
	C-005	Wuxi Shuangliang Biotechnology Co Ltd	Non-Small Cell Lung Cancer	Phase I
	cetuximab	Eli Lilly Canada Inc; Merck; Bristol-Myers Squibb KK; PT. Merck Tbk;	Head And Neck Cancer Squamous Cell Carcinoma; Metastatic Colorectal Cancer	Marketed
		Merck	Metastatic Colorectal Cancer	Phase I
		TheraOp gGmbH	Metastatic Colorectal Cancer	Phase II
		Eli Lilly and Co	Anal Cancer	Phase II
		Merck	Recurrent Head and Neck Cancer Squamous Cell Carcinoma; Squamous Non-Small Cell Lung Cancer	Phase II
	cetuximab + cobimetinib + palbociclib	Cothera Bioscience Pty Ltd	Metastatic Colorectal Cancer	Phase II
		Mabpharm Ltd	Metastatic Colorectal Cancer	Phase III

	cetuximab biobetter	Dragonboat Biopharmaceutical (Shanghai) Co Ltd; Shanghai Jing Ze Biotechnology Co Ltd	Cervical Cancer; Colorectal Cancer; Endometrial Cancer; Esophageal Squamous Cell Carcinoma (ESCC); Head and Neck Cancer Squamous Cell Carcinoma; Metastatic Colorectal Cancer; Ovarian Cancer; Penile Cancer	Phase I
		Enzene Biosciences Ltd	Head And Neck Cancer Squamous Cell Carcinoma; Lip Cancer; Locally Recurrent or Locoregional Solid Malignancies; Oral Cavity (Mouth) Cancer; Pharyngeal Neoplasm	Phase III
		Ampo Biotechnology Inc; Cinnagen Co; Sichuan Kelun Pharmaceutical Co Ltd; 3SBio Inc	Metastatic Colorectal Cancer	Phase III
		R-Pharm	Recurrent Head and Neck Cancer Squamous Cell Carcinoma	Phase III
	dabrafenib mesylate + panitumumab + trametinib dimethyl sulfoxide	Novartis AG	Metastatic Colorectal Cancer	Phase II
	dacomitinib	Pfizer	Non-Small Cell Lung Cancer	Marketed
			Human Epidermal Growth Factor Receptor 2 Positive Breast Cancer (HER2+ Breast Cancer); Ovarian Cancer; Triple-Negative Breast Cancer (TNBC)	Phase I

	DBPR-112	AnBogen Therapeutics	Non-Small Cell Lung Cancer; Solid Tumor	Phase II
	DF-203	Suzhou Dingfu Target Biotechnology Co Ltd	Colorectal Cancer; Head and Neck Cancer Squamous Cell Carcinoma; Non-Small Cell Lung Cancer; Pancreatic Cancer; Renal Cell Carcinoma; Solid Tumor; Triple-Negative Breast Cancer (TNBC)	Phase I
	doxitinib mesylate	Henan Genuine Biotech Co Ltd	Non-Small Cell Lung Cancer	Phase II
	DZD-9008	Dizal (Jiangsu) Pharmaceutical Co Ltd	Solid Tumor; Non-Small Cell Lung Cancer	Phase II
	EO-1001	Senz Oncology Pty Ltd	Unspecified Cancer	Phase II
		Edison Oncology Holding Corp	Breast Cancer; Central Nervous System (CNS) Cancer; Non-Small Cell Lung Cancer	Phase II
	epertinib	Shionogi & Co Ltd	Breast Cancer; Malignant Neoplasms	Phase II
		EOC Pharma Ltd	Breast Cancer	Phase II
		Hutchison MediPharma Ltd	Glioblastoma Multiforme (GBM)	Phase II
	ERAS-801	Erasca Inc	Recurrent Glioblastoma Multiforme (GBM)	Phase I
	erlotinib	More than 15 companies	Metastatic Pancreatic Cancer; Non-Small Cell Lung Cancer	Marketed
	erlotinib hydrochloride	More than 50 companies	Metastatic Pancreatic Cancer; Non-Small Cell Lung Cancer	Marketed

	ES-072	Zhejiang Bossan Pharmaceutical Co Ltd	Non-Small Cell Lung Cancer	Phase I
	FCN-411	Fochon Pharmaceutical Ltd	Head And Neck Cancer Squamous Cell Carcinoma	Phase I
			Non-Small Cell Lung Cancer	Phase II
	FHND-9041	Jiangsu Zhengda Fenghai Pharmaceutical Co Ltd	Non-Small Cell Lung Cancer	Phase III
	Fusion Protein to Antagonize EGFR for Glioblastoma Multiforme and Malignant Glioma	Istari Oncology Inc	Glioblastoma Multiforme (GBM); Malignant Glioma	Phase II
	FWD-1509	Shenzhen Forward Pharmaceutical Co Ltd	Non-Small Cell Lung Cancer	Phase II
	GB-263	Genor BioPharma Co Ltd	Non-Small Cell Lung Cancer; Solid Tumor; Esophageal Cancer; Gastric Cancer; Head and Neck Cancer Squamous Cell Carcinoma; Metastatic Colorectal Cancer	Phase II
	GC-1118A	GC Biopharma Corp	Adenocarcinoma Of the Gastroesophageal Junction; Colon Cancer; Gastric Cancer; Metastatic Colorectal Cancer; Solid Tumor	Phase II
	gefitinib	AstraZeneca; Daiichi Sankyo Espha Co Ltd	Non-Small Cell Lung Cancer	Marketed

	H-002	RedCloud Bio Inc	Non-Small Cell Lung Cancer	Phase II
	HL-07	Hualan Biological Engineering Inc	Metastatic Colorectal Cancer	Phase II
	HS-627	Zhejiang Hisun Pharmaceutical Co Ltd	Triple-Negative Breast Cancer (TNBC)	Phase I
			Human Epidermal Growth Factor Receptor 2 Positive Breast Cancer (HER2+ Breast Cancer)	Phase III
	icotinib hydrochloride	Betta Pharmaceuticals Co Ltd	Non-Small Cell Lung Cancer	Marketed
	JMT-101	CSPC Pharmaceutical Group Ltd	Esophageal Squamous Cell Carcinoma (ESCC); Metastatic Colorectal Cancer; Non-Small Cell Lung Cancer; Solid Tumor	Phase I
			Non-Small Cell Lung Cancer	Phase II
	JS-111	Shanghai Junshi Bioscience Co Ltd	Non-Small Cell Lung Cancer	Phase II
	KBP-5209	XuanZhu Biological Technology Co Ltd	Breast Cancer; Carcinoma of Unknown Primary (Occult Primary Tumor/Cancer of Unknown Primary); Colorectal Cancer; Gallbladder Cancer; Gastric Cancer; Head and Neck Cancer; Non-Small Cell Lung Cancer; Ovarian Cancer; Pancreatic Cancer; Paranasal Sinus And Nasal Cavity Cancer; Sarcomas	Phase II
	lapatinib	Lupin Pharmaceuticals Inc; Sayre Therapeutics	Human Epidermal Growth Factor Receptor 2 Positive Breast Cancer (HER2+ Breast Cancer)	Marketed

	lapatinib ditosylate	Zhuhai Rundu Pharmaceutical Co Ltd; Hetero Healthcare Ltd; Cipla Ltd	Human Epidermal Growth Factor Receptor 2 Positive Breast Cancer (HER2+ Breast Cancer)	Marketed
	larotinib	HEC Pharma Co Ltd	Esophageal Squamous Cell Carcinoma (ESCC)	Phase III
		Yuhan Corp	Non-Small Cell Lung Cancer	Marketed
		Genosco Inc	Metastatic Brain Tumor	Phase II
		Johnson & Johnson; Genosco Inc	Non-Small Cell Lung Cancer	Phase III
	lifirafenib maleate	BeiGene Ltd	Colorectal Cancer; Endometrial Cancer; Non-Small Cell Lung Cancer; Ovarian Cancer; Pancreatic Cancer; Cholangiocarcinoma; Melanoma; Papillary Thyroid Cancer;	Phase II
	LL-191	Nalo Therapeutics Inc	Non-Small Cell Lung Cancer	Phase I
	MCLA-129	Merus NV; Betta Pharmaceuticals Co Ltd	Adenocarcinoma Of the Gastroesophageal Junction; Esophageal Squamous Cell Carcinoma (ESCC); Gastric Cancer; Head And Neck Cancer Squamous Cell Carcinoma; Non-Small Cell Lung Cancer	Phase II
	MET-306	Huadong Medicine Co Ltd	Non-Small Cell Lung Cancer	Phase III
	mobocertinib		Non-Small Cell Lung Cancer	Marketed

		Takeda Pharmaceuticals Australia Pty Ltd	Bladder Cancer; Breast Cancer; Esophageal Cancer; Gastric Cancer; Head and Neck Cancer; Metastatic Biliary Tract Cancer; Urinary Tract Cancer	Phase II
			Non-Small Cell Lung Cancer	Phase III
	MVC-101	Maverick Therapeutics Inc	Colorectal Cancer; Head and Neck Cancer Squamous Cell Carcinoma; Non-Small Cell Lung Cancer; Pancreatic Cancer; Solid Tumor	Phase II
	naquotinib mesylate	Novartis AG	Non-Small Cell Lung Cancer	Phase II
	necitumumab	Nippon Kayaku Co Ltd; Eli Lilly Canada Inc Biotech Pharmaceutical Co Ltd PT Kalbe Farma Tbk	Squamous Non-Small Cell Lung Cancer	Marketed
			Nasopharyngeal Cancer	Marketed
			High-Grade Glioma	Marketed
		Biocon Ltd	Head And Neck Cancer Squamous Cell Carcinoma	Marketed
		Eurofarma Laboratorios SA	Glioma; High-Grade Glioma; Pediatric Diffuse Intrinsic Pontine Glioma	Marketed
		Biotech Pharmaceutical Co Ltd	Recurrent Head and Neck Cancer Squamous Cell Carcinoma	Phase I
		Biotech Pharmaceutical Co Ltd	Head And Neck Cancer Squamous Cell Carcinoma	Phase II

		InnoMab Pte Ltd	Cervical Cancer	Phase III
		Biotech Pharmaceutical Co Ltd	Pediatric Diffuse Intrinsic Pontine Glioma	Phase III
	NRC-2694	Natco Pharma Ltd	Hypopharyngeal Cancer; Laryngeal Cancer; Oral Cavity (Mouth) Cancer; Oropharyngeal Cancer; Recurrent Head and Neck Cancer Squamous Cell Carcinoma	Phase II
	olafertinib	Checkpoint Therapeutics Inc; Suzhou Neupharma Co Ltd	Non-Small Cell Lung Cancer	Phase II
	olmutinib hydrochloride	Hanmi Pharmaceuticals Co Ltd	Non-Small Cell Lung Cancer	Marketed
	osimertinib mesylate	AstraZeneca	Non-Small Cell Lung Cancer	Marketed
	panitumumab	Amgen; PT Glaxo Wellcome; Takeda Pharmaceutical Co Ltd; Amgen Inc; Dr. Reddy's Laboratories Ltd	Metastatic Colorectal Cancer	Marketed

	PB-357	Puma Biotechnology Inc	Breast Cancer	Phase I
	petosemtamab	Merus NV	Metastatic Colorectal Cancer; Solid Tumor	Phase II
	poziotinib hydrochloride	Hanmi Pharmaceuticals Co Ltd	Esophageal Cancer	Phase I
			Human Epidermal Growth Factor Receptor 2 Positive Breast Cancer (HER2+ Breast Cancer); Lung Adenocarcinoma	Phase II
			Non-Small Cell Lung Cancer	Phase III
	pyrotinib	Jiangsu Hengrui Medicine Co Ltd	Human Epidermal Growth Factor Receptor 2 Positive Breast Cancer (HER2+ Breast Cancer)	Marketed
	QL-1105	Qilu Pharmaceutical Co Ltd	Colorectal Cancer; Head and Neck Cancer	Phase I
	QL-1203	Qilu Pharmaceutical Co Ltd	Metastatic Colorectal Cancer	Phase III
	RXDX-105	F. Hoffmann-La Roche Ltd	Leptomeningeal Disease (Neoplastic Meningitis, Leptomeningeal Carcinomatosis); Lung Adenocarcinoma; Medullary Thyroid Cancer; Ovarian Cancer; Solid Tumor; Squamous Non-Small Cell Lung Cancer	Phase I
	sapitinib	AstraZeneca Plc	Metastatic Colorectal Cancer	Phase III
	SCT-200	SinoCelltech Group Ltd	Colorectal Cancer	Phase I
			Recurrent Head and Neck Cancer Squamous Cell Carcinoma	Phase II

			Esophageal Squamous Cell Carcinoma (ESCC); Metastatic Colorectal Cancer; Triple-Negative Breast Cancer (TNBC)	Phase II
	selatinib ditosilate	Qilu Pharmaceutical Co Ltd	Breast Cancer	Phase I
	sirotinib	XuanZhu Biological Technology Co Ltd	Esophageal Squamous Cell Carcinoma (ESCC); Gastric Cancer; Lung Cancer	Phase I
	SKLB-1028	CSPC Pharmaceutical Group Ltd	Acute Myelocytic Leukemia (AML, Acute Myeloblastic Leukemia)	Phase II
			Refractory Acute Myeloid Leukemia; Relapsed Acute Myeloid Leukemia	Phase III
	SPH-118811	Shanghai Pharmaceutical Group Co Ltd	Non-Small Cell Lung Cancer	Phase I
	Sutetinib maleate	Suzhou Teligene Ltd	Non-Small Cell Lung Cancer	Phase II
	SYHA-12128	CSPC Pharmaceutical Group Ltd	Adenocarcinoma Of the Gastroesophageal Junction; Colorectal Cancer; Gastric Cancer	Phase I
			Bile Duct Cancer (Cholangiocarcinoma); Extrahepatic Bile Duct Cancer; Gallbladder Cancer; Metastatic Biliary Tract Cancer; Medullary Thyroid Cancer; Non-Small Cell Lung Cancer	Phase II
	SYN-004	Synermore Biologics Co Ltd	Head And Neck Cancer Squamous Cell Carcinoma; Metastatic Colorectal Cancer; Non-Small Cell Lung Cancer; Solid Tumor	Phase I

	TAS-2940	Taiho Oncology Inc	Glioblastoma Multiforme (GBM); Human Epidermal Growth Factor Receptor 2 Positive Breast Cancer (HER2+ Breast Cancer); Non-Small Cell Lung Cancer	Phase I
	tesevatinib tosylate	Kadmon Holdings Inc	Leptomeningeal Disease (Neoplastic Meningitis, Leptomeningeal Carcinomatosis); Metastatic Brain Tumor; Recurrent Glioblastoma Multiforme (GBM); Non-Small Cell Lung Cancer	Phase II
	tomuzotuximab	Glycotope GmbH	Breast Cancer; Esophageal Cancer; Gastric Cancer; Gynecological Cancer; Kidney Cancer (Renal Cell Cancer); Metastatic Colorectal Cancer; Non-Small Cell Lung Cancer	Phase I
			Recurrent Head and Neck Cancer Squamous Cell Carcinoma	Phase II
	TQB-3804	Chia Tai Tianqing Pharmaceutical Group Co Ltd	Malignant Neoplasms	Phase I
	Vaccine	Center of Molecular Immunology	Hormone Refractory (Castration Resistant, Androgen-Independent) Prostate Cancer	Phase I
	vandetanib	Sanofi-Aventis (Suisse); Medley Industria Farmaceutica Ltda; Genzyme Europe BV	Medullary Thyroid Cancer	Marketed
	varlitinib	Aslan Pharmaceuticals Ltd	Bladder Cancer; Breast Cancer; Colorectal Cancer; Gastrointestinal Tumor; Glioblastoma Multiforme (GBM); Head and Neck Cancer Squamous Cell Carcinoma; Hepatobiliary System Tumor; Metastatic Hepatocellular	Phase I

			Carcinoma (HCC); Non-Small Cell Lung Cancer; Ovarian Cancer; Pancreatic Cancer; Prostate Cancer	
			Gastric Cancer; Human Epidermal Growth Factor Receptor 2 Positive Breast Cancer (HER2+ Breast Cancer); Gallbladder Cancer	Phase II
			Gastroesophageal (GE) Junction Carcinomas; Cholangiocarcinoma	Phase III
			Papillary Thyroid Cancer; Solid Tumor	Phase III
	VRN-07	Voronoi Group	Solid Tumor	Phase I
	WJ-13404	Wigen Biomedicine Technology (Shanghai) Co Ltd	Non-Small Cell Lung Cancer	Phase II
	WSD-0922	Wayshine Biopharma Inc	Non-Small Cell Lung Cancer; Anaplastic Astrocytoma; Glioblastoma Multiforme (GBM)	Phase I
	XZP-5809	Sihuan Pharmaceutical Holdings Group Ltd	Non-Small Cell Lung Cancer	Phase I
	yinlitinib	HEC Pharma Co Ltd	Breast Cancer	Phase I
	YZJ-0318	Yangtze River Pharmaceutical Group	Non-Small Cell Lung Cancer	Phase I
	zipalertinib	Taiho Pharmaceutical Co Ltd; Zai Lab Ltd	Non-Small Cell Lung Cancer	Phase II

	ZNE-4	Zentalis Pharmaceuticals Inc	Non-Small Cell Lung Cancer	Phase II
	zorifertinib	Alpha Biopharma Ltd	Non-Small Cell Lung Cancer	Phase III
PGF [116]	conbercept	Chengdu Kanghong Pharmaceuticals Group Co Ltd	Retinoblastoma	Phase II
	ziv-aflibercept	Sanofi-Aventis	Metastatic Colorectal Cancer	Marketed
	ziv-aflibercept	Regeneron Pharmaceuticals Inc	Uveal Melanoma	Phase II
	THR-317	Oncurious NV	Medulloblastoma	Phase II
	ziv-aflibercept biosimilar	Luye Pharma Group Ltd	Metastatic Colorectal Cancer	Phase II
CXCL8 [194]	BMS-986253	Bristol-Myers Squibb Co	Head And Neck Cancer Squamous Cell Carcinoma; Hepatocellular Carcinoma; Hormone-Sensitive Prostate Cancer; Melanoma; Non-Small Cell Lung Cancer; Solid Tumor	Phase II
			Melanoma; Renal Cell Carcinoma	Phase I
ITGA2 [195]	E-7820	Eisai Co Ltd	Chronic Myelomonocytic Leukemia (CMML); Myelodysplastic Syndrome; Refractory Acute Myeloid Leukemia; Relapsed Acute Myeloid Leukemia	Phase II
HK2 [196]	tuvatexib	Vidac Pharma	Cutaneous T-Cell Lymphoma	Phase II

HMGB1 [197]	dociparstat sodium	Chimerix Inc	Acute Myelocytic Leukemia (AML, Acute Myeloblastic Leukemia)	Phase III
CLDN1 [198]	ALEF-02	Alentis Therapeutics AG	Solid Tumor	Phase I
VEGFA [199]	ABL-001	Compass Therapeutics Inc	Extrahepatic Bile Duct Cancer; Gallbladder Cancer; Metastatic Biliary Tract Cancer; Metastatic Colorectal Cancer	Phase I
		Handok Inc; Elpiscience Biopharma Ltd	Bile Duct Cancer (Cholangiocarcinoma); Extrahepatic Bile Duct Cancer; Gallbladder Cancer; Gastric Cancer; Gastrointestinal Stromal Tumor (GIST); Metastatic Colorectal Cancer; Non-Small Cell Lung Cancer; Ovarian Cancer; Pancreatic Cancer; Solid Tumor	Phase II
	bevacizumab	Roche; Chugai Pharmaceutical Co Ltd; Genentech; Cipla; PT Boehringer Ingelheim	Cervical Cancer; Epithelial Ovarian Cancer; Fallopian Tube Cancer; Metastatic Breast Cancer; Metastatic Colorectal Cancer; Metastatic Renal Cell Carcinoma; Non-Small Cell Lung Cancer; Peritoneal Cancer	Marketed
	bevacizumab	Chugai Pharmaceutical Co Ltd; F. Hoffmann-La Roche Ltd	Hepatocellular Carcinoma; Human Epidermal Growth Factor Receptor 2 Negative Breast Cancer (HER2- Breast Cancer)	Phase II
	bevacizumab	Chugai Pharmaceutical Co Ltd; F. Hoffmann-La Roche Ltd	Cervical Cancer; Malignant Pleural Mesothelioma; Melanoma; Hepatocellular Carcinoma; Metastatic Colorectal Cancer; Lung Cancer; Human Epidermal Growth Factor Receptor 2 Negative Breast Cancer (HER2- Breast Cancer)	Phase III

	bevacizumab + paclitaxel	Sorrento Therapeutics Inc	Adenocarcinoma; Cervical Cancer; Clear Cell Squamous Cell Carcinoma; Endometrial Cancer; Fallopian Tube Cancer; Melanoma; Ovarian Cancer; Peritoneal Cancer; Squamous Cell Carcinoma	Phase I
	bevacizumab biosimilar	Pfizer; Amgen Inc; Daiichi Sankyo Co Ltd; PT Pyridam Farma Tbk; BeiGene Ltd; Cipla; Celltrion Inc; Eris Lifesciences Ltd; Biocad; Qilu Pharmaceutical Co Ltd; Merck	Epithelial Ovarian Cancer; Fallopian Tube Cancer; Glioblastoma Multiforme (GBM); Metastatic Colorectal Cancer; Non-Small Cell Lung Cancer; Peritoneal Cancer; Cervical Cancer; Fallopian Tube Cancer; Metastatic Breast Cancer; Metastatic Renal Cell Carcinoma; Peritoneal Cancer	Marketed
	ziv-aflibercept	Sanofi-Aventis	Metastatic Colorectal Cancer	Marketed
		Regeneron Pharmaceuticals Inc	Uveal Melanoma	Phase II
	ziv-aflibercept biosimilar	Luye Pharma Group Ltd	Metastatic Colorectal Cancer	Phase II
TFRC	CX-2029	CytomX Therapeutics Inc	Diffuse Large B-Cell Lymphoma; Squamous Non-Small Cell Lung Cancer. Adenoid Cystic Carcinoma (ACC); Bladder Cancer; Colorectal Cancer; Esophageal Cancer; Gastroesophageal (GE) Junction Carcinomas; Head and Neck Cancer Squamous Cell Carcinoma; Hepatocellular Carcinoma; Kidney Cancer (Renal Cell Cancer); Malignant Pleural Mesothelioma; Ocular Melanoma; Ovarian Cancer; Pancreatic Cancer; Prostate Cancer; Soft Tissue	Phase II

			Sarcoma; Solid Tumor; Thymic Carcinoma; Thymoma (Thymic Epithelial Tumor); Thyroid Cancer	
	INA-03	Inatherys	Acute Lymphocytic Leukemia (ALL, Acute Lymphoblastic Leukemia); Acute Myelocytic Leukemia (AML, Acute Myeloblastic Leukemia); Leukemia; Refractory Acute Myeloid Leukemia; Relapsed Acute Myeloid Leukemia	Phase I
	JSTTFR-09	Fujifilm Holdings Corp	Polycythemia Vera	Phase I
PFKFB3 [200]	KAN-0438757	Kancera AB	Triple-Negative Breast Cancer (TNBC)	Preclinical
CIB1 [201-203]	Small Molecules	Reveris Therapeutics LLC	Breast Cancer	Preclinical
HSP90AA1 [204]	Small Molecule	China Medical University	Unspecified Cancer	Preclinical

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