

Supplemental Table S1a. Genes included in Guardant360® panel and related genotype-directed therapy.

<i>CfDNA mutation</i>	<i>Corresponding genotype-directed therapy*</i>
<i>AKT1</i>	mTOR inhibitor
<i>ALK</i>	ALK/RET inhibitor, ALK/ROS1/IGF-1R/FLT-3/EGFR inhibitor, ALK/IGF-1R/InsR/ROS1 inhibitor, ALK/c-Met/ROS1/RON inhibitor
<i>APC</i>	COX-2 inhibitor
<i>AR</i>	Anti-androgen therapy
<i>ARAF</i>	Multi-kinase inhibitor, MEK inhibitor, MAPK/MEK inhibitor
<i>ARID1A</i>	None
<i>ATM</i>	DNA damage repair pathway inhibition (PARP inhibition, DNA damaging chemotherapy)
<i>BRAF</i>	Multi-kinase inhibitor, MEK inhibitor, MAPK/MEK inhibitor
<i>BRCA1</i>	DNA damage repair pathway inhibition (PARP inhibition, DNA damaging chemotherapy)
<i>BRCA2</i>	DNA damage repair pathway inhibition (PARP inhibition, DNA damaging chemotherapy)
<i>CCND1</i>	CDK4/6 inhibitor
<i>CCND2</i>	CDK4/6 inhibitor
<i>CCNE1</i>	None
<i>CDH1</i>	None
<i>CDK4</i>	CDK4/6 inhibitor
<i>CDK6</i>	CDK4/6 inhibitor
<i>CDKN2A</i>	CDK4/6 inhibitor
<i>CTNNB1</i>	COX-2 inhibitor
<i>DDR2</i>	None
<i>EGFR</i>	EGFR inhibitor, EGFR/HER2/HER4 inhibitor, EGFR/HER2 inhibitor
<i>ERBB2</i>	HER2 (ERBB2) inhibitor EGFR/HER2/HER4 inhibitor, EGFR/HER2 inhibitor
<i>ESR1</i>	SERD
<i>EZH2</i>	Histone deacetylase (HDAC) inhibitor,

	Anti-epileptic
<i>FBXW7</i>	mTOR inhibitor
<i>FGFR1</i>	VEGFR inhibitor, Multi-kinase inhibitor, VEGF/PDGFR/FGFR/Kit/Itk/Lck/c-Fms inhibitor, PDGFR/FGFR/VEGFR/FLT3 inhibitor
<i>FGFR2</i>	VEGFR inhibitor, Multi-kinase inhibitor, VEGF/PDGFR/FGFR/Kit/Itk/Lck/c-Fms inhibitor, PDGFR/FGFR/VEGFR/FLT3 inhibitor
<i>FGFR3</i>	VEGF/PDGFR/FGFR/Kit/Itk/Lck/c-Fms inhibitor, VEGFR inhibitor, PDGFR/FGFR/VEGFR/FLT3 inhibitor, Multi-kinase inhibitor
<i>GATA3</i>	None
<i>GNA11</i>	MEK inhibitor, MAPK/MEK inhibitor
<i>GNAQ</i>	MEK inhibitor, MAPK/MEK inhibitor
<i>GNAS</i>	MEK inhibitor, MAPK/MEK inhibitor
<i>HNF1A</i>	None
<i>HRAS</i>	MEK inhibitor, MAPK/MEK inhibitor
<i>IDH1</i>	DNA methylation inhibitor
<i>IDH2</i>	DNA methylation inhibitor IDH2 inhibitor
<i>JAK2</i>	JAK inhibitor
<i>JAK3</i>	JAK inhibitor
<i>KIT</i>	VEGFR inhibitor, mTOR inhibitor, BCR-ABL tyrosine kinase inhibitor, Multi-kinase inhibitor, PDGFR/VEGFR/KIT/FLT3/CSF-1R/RET inhibitor, VEGF/PDGFR/FGFR/Kit/Itk/Lck/c-Fms inhibitor, BCR-ABL/SRC family/c-KIT/EPHA2/PDGFR inhibitor
<i>KRAS</i>	MEK inhibitor, MAPK/MEK inhibitor

<i>MAP2K1</i>	MEK inhibitor, MAPK/MEK inhibitor
<i>MAP2K2</i>	MEK inhibitor, MAPK/MEK inhibitor
<i>MAPK1</i>	EGFR inhibitor
<i>MAPK3</i>	None
<i>MET</i>	Multi-kinase inhibitor, ALK/c-Met/ROS1/RON inhibitor
<i>MLH1</i>	Immunotherapy
<i>MPL</i>	JAK inhibitor, AKT inhibitor
<i>MTOR</i>	mTOR inhibitor
<i>MYC</i>	None
<i>NF1</i>	mTOR inhibitor, MEK inhibitor, MAPK/MEK inhibitor
<i>NFE2L2</i>	mTOR inhibitor
<i>NOTCH1</i>	None
<i>NPM1</i>	None
<i>NRAS</i>	MEK inhibitor, MAPK/MEK inhibitor
<i>NTRK1</i>	ALK/c-Met/ROS1/RON inhibitor (crizotinib)
<i>NTRK3</i>	ALK/c-Met/ROS1/RON inhibitor (crizotinib)
<i>PDGFRA</i>	VEGFR inhibitor, BCR-ABL tyrosine kinase inhibitor, PDGFR/VEGFR/KIT/FLT3/CSF-1R/RET inhibitor, Multi-kinase inhibitor, VEGF/PDGFR/FGFR/Kit/Itk/Lck/c-Fms inhibitor, PDGFR inhibitor, BCR-ABL/SRC family/c-KIT/EPHA2/PDGFR inhibitor, PDGFR/FGFR/VEGFR/FLT3 inhibitor, mTOR inhibitor
<i>PIK3CA</i>	mTOR inhibitor, PI3K inhibitor
<i>PTEN</i>	mTOR inhibitor, PI3K inhibitor
<i>PTPN11</i>	MEK inhibitor, MAPK/MEK inhibitor
<i>RAF1</i>	MEK inhibitor, Multi-kinase inhibitor, MAPK/MEK inhibitor

<i>RBI</i>	None
<i>RET</i>	VEGFR inhibitor, Multi-kinase inhibitor, EGFR/VEGF/RET/BRK/TIE2/EPH/Src kinase family/Src family inhibitor
<i>RHEB</i>	mTOR inhibitor
<i>RHOA</i>	mTOR inhibitor
<i>RITI</i>	mTOR inhibitor, MEK inhibitor, MAPK/MEK inhibitor
<i>ROS1</i>	ALK/c-Met/ROS1/RON inhibitor, Multi-kinase inhibitor
<i>SMAD4</i>	None
<i>SMO</i>	Hedgehog pathway inhibitor
<i>STK11</i>	mTOR inhibitor, BCR-ABL tyrosine kinase inhibitor, BCR-ABL/SRC family/c-KIT/EPHA2/PDGFR inhibitor
<i>TERT</i>	None
<i>TP53</i>	None
<i>TSC1</i>	mTOR inhibitor
<i>VHL</i>	VEGF inhibitor, VEGF/PDGFR/FGFR/Kit/Itk/Lck/c-Fms inhibitor, Multi-kinase inhibitor, PDGFR/VEGFR/KIT/FLT3/CSF-1R/RET inhibitor, VEGFR inhibitor, mTOR inhibitor, EGFR/VEGF/RET/BRK/TIE2/EPH/Src kinase family/Src family inhibitor

***Genotype-directed therapy designation modified from Guardant360[®] classification, as described in the methodology of this manuscript. For all mutations, genotype-directed clinical trials (if available) were also considered.**

Supplemental Table S1b. Genes included in institutional SNaPshot panel.

<i>ABL1</i>
<i>AKT1</i>
<i>ALK</i>
<i>APC</i>
<i>ARID1A</i>

<i>ATM</i>
<i>ATRX</i>
<i>AURKA</i>
<i>BRAF</i>
<i>BRCA1</i>
<i>BRCA2</i>
<i>CCNE1</i>
<i>CDH1</i>
<i>CDK4</i>
<i>CDKN2A</i>
<i>CIC</i>
<i>CSF1R</i>
<i>CTNNB1</i>
<i>DAXX</i>
<i>DDR2</i>
<i>DDX3X</i>
<i>EGFR</i>
<i>ERBB2</i>
<i>ERBB3</i>
<i>ERBB4</i>
<i>ESR1</i>
<i>EZH2</i>
<i>FBXW7</i>
<i>FGFR1</i>
<i>FGFR2</i>
<i>FGFR3</i>
<i>FLT3</i>
<i>FOXL2</i>
<i>GNAI1</i>
<i>GNAQ</i>
<i>GNAS</i>
<i>H3F3A</i>
<i>HNF1A</i>
<i>HRAS</i>
<i>IDH1</i>
<i>IDH2</i>
<i>JAK2</i>
<i>JAK3</i>

<i>KDR</i>
<i>KEAP1</i>
<i>KIT</i>
<i>KRAS</i>
<i>MAP2K1</i>
<i>MAP3K1</i>
<i>MDM2</i>
<i>MEN1</i>
<i>MET</i>
<i>MLH1</i>
<i>MPL</i>
<i>MSH6</i>
<i>MSI</i>
<i>MYC</i>
<i>MYCN</i>
<i>NF1</i>
<i>NF2</i>
<i>NOTCH1</i>
<i>NPM1</i>
<i>NRAS</i>
<i>PIK3CA</i>
<i>PIK3R1</i>
<i>POLE</i>
<i>PTCH1</i>
<i>PTEN</i>
<i>PTPN11</i>
<i>RB1</i>
<i>RET</i>
<i>RHOA</i>
<i>RNF43</i>
<i>ROS1</i>
<i>SDHB</i>
<i>SMAD2</i>
<i>SMAD4</i>
<i>SMARCA4</i>
<i>SMARCB1</i>
<i>SMO</i>
<i>SRC</i>

<i>STAG2</i>
<i>STK11</i>
<i>SUFU</i>
<i>TERT</i>
<i>TP53</i>
<i>TP63</i>
<i>TSC1</i>
<i>TSC2</i>
<i>TSHR</i>
<i>VHL</i>