

# Technical Specifications



## Intended Use

FoundationOne®CDx is a qualitative next-generation sequencing based *in vitro* diagnostic test that uses targeted high throughput hybridization-based capture technology for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients who may benefit from treatment with the targeted therapies listed in Table 1 in accordance with the approved therapeutic product labeling. Additionally, FoundationOne CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms. Genomic findings other than those listed in Table 1 are not prescriptive or conclusive for labeled use of any specific therapeutic product.

**Table 1: Companion Diagnostic Indications**

TUMOR TYPE	BIOMARKE(S) DETECTED	THERAPY
Breast Cancer	<i>AKT1</i> E17K; <i>PIK3CA</i> R88Q, N345K, C420R, E542K, E545A, E545D, E545Q, E545K, E545G, Q546E, Q546K, Q546R, Q546P, M1043V, M1043I, H1047Y, H1047R, H1047L, and G1049R; and <i>PTEN</i> alterations	TRUQAP™ (capivasertib) in combination with FASLODEX® (fulvestrant)
	<i>ERBB2</i> (HER2) amplification	HERCEPTIN® (trastuzumab)
		KADCYLA® (ado-trastuzumab emtansine)
		PERJETA® (pertuzumab)
	<i>PIK3CA</i> C420R, E542K, E545A, E545D [1635G>T only], E545G, E545K, Q546E, Q546R, H1047L, H1047R, and H1047Y alterations	PIQRAY® (alpelisib)
Cholangiocarcinoma	<i>FGFR2</i> fusions and select rearrangements	PEMAZYRE® (pemigatinib)
Colorectal Cancer	<i>KRAS</i> wild-type (absence of mutations in codons 12 and 13)	ERBITUX® (cetuximab)
	<i>KRAS</i> wild-type (absence of mutations in exons 2, 3 and 4) and <i>NRAS</i> wild-type (absence of mutations in exons 2, 3 and 4)	VECTIBIX® (panitumumab)
Melanoma	<i>BRAF</i> V600 mutation-positive	TECENTRIQ® (atezolizumab) in combination with COTELLIC® (cobimetinib) and ZELBORAF® (vemurafenib)
	<i>BRAF</i> V600E	BRAF Inhibitor Approved by FDA*
	<i>BRAF</i> V600E and V600K	BRAF/MEK Inhibitor Combinations Approved by FDA*
		MEKINIST® (trametinib)
Non-Small Cell Lung Cancer (NSCLC)	<i>ALK</i> rearrangements	ALECENSA® (alectinib)
		ALUNBRIG® (brigatinib)
		XALKORI® (crizotinib)
		ZYKADIA® (ceritinib)
	<i>BRAF</i> V600E	BRAFTOVI® (encorafenib) in combination with MEKTOVI® (binimetinib)
		TAFINLAR® (dabrafenib) in combination with MEKINIST® (trametinib)
	<i>EGFR</i> exon 19 deletions and <i>EGFR</i> exon 21 L858R alterations	EGFR Tyrosine Kinase Inhibitors (TKI) Approved by FDA*
	<i>EGFR</i> exon 20 T790M alterations	TAGRISSO® (osimertinib)
	<i>MET</i> single nucleotide variants (SNVs) and indels that lead to <i>MET</i> exon 14 skipping	TABRECTA® (capmatinib)
	<i>ROS1</i> fusions	ROZLYTREK® (entrectinib)
Ovarian Cancer	<i>BRCA1</i> , <i>BRCA2</i> alterations	LYNPARZA® (olaparib)
Pediatric Low-Grade Glioma	<i>BRAF</i> V600 mutation-positive and <i>BRAF</i> fusions	OJEMDA™ (tovorafenib)

TUMOR TYPE	BIOMARKE(S) DETECTED	THERAPY
Prostate Cancer	<i>BRCA1, BRCA2</i> alterations	AKEEGA® (niraparib + abiraterone acetate)
		LYNPARZA® (olaparib) in combination with abiraterone
	Homologous Recombination Repair (HRR) gene ( <i>BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D</i> and <i>RAD54L</i> ) alterations	LYNPARZA® (olaparib)
Solid Tumors	MSI-High	KEYTRUDA® (pembrolizumab)
	<i>NTRK1/2/3</i> fusions	ROZLYTREK® (entrectinib)
		VITRAKVI® (larotrectinib)
	<i>RET</i> fusions	RETEVMO® (selpercatinib)
	TMB ≥ 10 mutations per megabase	KEYTRUDA® (pembrolizumab)

\* For the most current information about the therapeutic products in this group, go to: <https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools>

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## Summary of Clinical Studies

Follow-on CDx claims were based on a non-inferiority statistical testing approach using the enrichment design presented in the paper by Li (2016).<sup>1</sup> All studies passed the acceptance criteria specific in each study protocol.

BIOMARKER	POSITIVE PERCENT AGREEMENT (PPA)†	NEGATIVE PERCENT AGREEMENT (NPA)	COMPARATOR METHOD‡
<i>EGFR</i> Exon 19 Deletions and L858R	98.1% (106/108)	99.4% (153/154)	cobas® <i>EGFR</i> Mutation Test v2
<i>EGFR</i> T790M	98.9% (87/88)	86.1% (93/108)	cobas® <i>EGFR</i> Mutation Test v1 cobas® <i>EGFR</i> Mutation Test v2
<i>ALK</i> Rearrangements	92.9% (78/84)	100% (75/75)	Ventana <i>ALK</i> (D5F3) CDx Assay Vysis <i>ALK</i> Break-Apart FISH Probe Kit
<i>KRAS</i>	100% (173/173)	100% (154/154)	therascreen® <i>KRAS</i> RGQ PCR Kit
<i>ERBB2</i> (HER2) Amplifications	89.4% (101/113)	98.4% (180/183)	Dako HER2 FISH PharmDx® Kit
<i>BRAF</i> V600	99.4% (166/167)	89.6% (121/135)§	cobas® <i>BRAF</i> V600 Mutation Test
<i>BRAF</i> V600E	99.3% (149/150)	99.2% (121/122)	
<i>BRAF</i> V600 dinucleotide¶	96.3% (26/27)	100% (24/24)	THxID® <i>BRAF</i> kit

\* For the most current information about the therapeutic products in this group, go to: <https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools>

† Cobas® is a trademark of Roche Diagnostics Operations, Inc. Therascreen® is a trademark of Qiagen. PharmDx® is a registered trademark of Dako Denmark A/S. THxID® is a registered trademark of bioMérieux.

‡ The reference standard used to calculate PPA and NPA is defined as the consensus calls between the two comparator methods - PPA being when FoundationOne CDx and the comparator method(s) identified mutations in mutated patients and NPA being when FoundationOne CDx and the comparator method(s) did not identify mutations in non-mutated patients.

§ Sensitivity of dinucleotide detection of *BRAF* V600K and V600E was found to be significantly reduced in cobas® test, in particular for samples in which FoundationOne CDx detected the dinucleotides to be of lower than 40% mutant allele frequency (MAF), leading to low NPA values.

¶ A study using the THxID® *BRAF* kit (bioMérieux) was conducted with samples with *BRAF* V600 dinucleotide mutation detected by FoundationOne CDx and *BRAF* V600 negative samples to provide a better evaluation of V600 dinucleotide concordance.



## Current Gene List<sup>2</sup>

Genes with full coding exonic regions included in FoundationOne®CDx for the detection of substitutions, insertion-deletions (indels), and copy-number alterations (CNAs).

<i>ABL1</i>	<i>ACVR1B</i>	<i>AKT1</i>	<i>AKT2</i>	<i>AKT3</i>	<i>ALK</i>	<i>ALOX12B</i>	<i>AMER1 (FAM123B)</i>	<i>APC</i>
<i>AR</i>	<i>ARAF</i>	<i>ARFRP1</i>	<i>ARID1A</i>	<i>ASXL1</i>	<i>ATM</i>	<i>ATR</i>	<i>ATRX</i>	<i>AURKA</i>
<i>AURKB</i>	<i>AXIN1</i>	<i>AXL</i>	<i>BAP1</i>	<i>BARD1</i>	<i>BCL2</i>	<i>BCL2L1</i>	<i>BCL2L2</i>	<i>BCL6</i>
<i>BCOR</i>	<i>BCORL1</i>	<i>BRAF</i>	<i>BRCA1</i>	<i>BRCA2</i>	<i>BRD4</i>	<i>BRIP1</i>	<i>BTG1</i>	<i>BTG2</i>
<i>BTK</i>	<i>C11ORF30 (EMSY)</i>	<i>CALR</i>	<i>CARD11</i>	<i>CASP8</i>	<i>CBFB</i>	<i>CBL</i>	<i>CCND1</i>	<i>CCND2</i>
<i>CCND3</i>	<i>CCNE1</i>	<i>CD22</i>	<i>CD274 (PD-L1)</i>	<i>CD70</i>	<i>CD79A</i>	<i>CD79B</i>	<i>CDC73</i>	<i>CDH1</i>
<i>CDK12</i>	<i>CDK4</i>	<i>CDK6</i>	<i>CDK8</i>	<i>CDKN1A</i>	<i>CDKN1B</i>	<i>CDKN2A</i>	<i>CDKN2B</i>	<i>CDKN2C</i>
<i>CEBPA</i>	<i>CHEK1</i>	<i>CHEK2</i>	<i>CIC</i>	<i>CREBBP</i>	<i>CRKL</i>	<i>CSF1R</i>	<i>CSF3R</i>	<i>CTCF</i>
<i>CTNNA1</i>	<i>CTNNB1</i>	<i>CUL3</i>	<i>CUL4A</i>	<i>CXCR4</i>	<i>CYP17A1</i>	<i>DAXX</i>	<i>DDR1</i>	<i>DDR2</i>
<i>DIS3</i>	<i>DNMT3A</i>	<i>DOT1L</i>	<i>EED</i>	<i>EGFR</i>	<i>EP300</i>	<i>EPHA3</i>	<i>EPHB1</i>	<i>EPHB4</i>
<i>ERBB2</i>	<i>ERBB3</i>	<i>ERBB4</i>	<i>ERCC4</i>	<i>ERG</i>	<i>ERRF1</i>	<i>ESR1</i>	<i>EZH2</i>	<i>FAM46C</i>
<i>FANCA</i>	<i>FANCC</i>	<i>FANCG</i>	<i>FANCL</i>	<i>FAS</i>	<i>FBXW7</i>	<i>FGF10</i>	<i>FGF12</i>	<i>FGF14</i>
<i>FGF19</i>	<i>FGF23</i>	<i>FGF3</i>	<i>FGF4</i>	<i>FGF6</i>	<i>FGFR1</i>	<i>FGFR2</i>	<i>FGFR3</i>	<i>FGFR4</i>
<i>FH</i>	<i>FLCN</i>	<i>FLT1</i>	<i>FLT3</i>	<i>FOXL2</i>	<i>FUBP1</i>	<i>GABRA6</i>	<i>GATA3</i>	<i>GATA4</i>
<i>GATA6</i>	<i>GID4 (C17ORF39)</i>	<i>GNA11</i>	<i>GNA13</i>	<i>GNAQ</i>	<i>GNAS</i>	<i>GRM3</i>	<i>GSK3B</i>	<i>H3F3A</i>
<i>HDAC1</i>	<i>HGF</i>	<i>HNFI1A</i>	<i>HRAS</i>	<i>HSD3B1</i>	<i>ID3</i>	<i>IDH1</i>	<i>IDH2</i>	<i>IGF1R</i>
<i>IKBKE</i>	<i>IKZF1</i>	<i>INPP4B</i>	<i>IRF2</i>	<i>IRF4</i>	<i>IRS2</i>	<i>JAK1</i>	<i>JAK2</i>	<i>JAK3</i>
<i>JUN</i>	<i>KDM5A</i>	<i>KDM5C</i>	<i>KDM6A</i>	<i>KDR</i>	<i>KEAP1</i>	<i>KEL</i>	<i>KIT</i>	<i>KLHL6</i>



## Current Gene List Continued<sup>2</sup>

KMT2A (MLL)	KMT2D (MLL2)	KRAS	LTK	LYN	MAF	MAP2K1 (MEK1)	MAP2K2 (MEK2)	MAP2K4
MAP3K1	MAP3K13	MAPK1	MCL1	MDM2	MDM4	MED12	MEF2B	MEN1
MERTK	MET	MITF	MKNK1	MLH1	MPL	MRE11A	MSH2	MSH3
MSH6	MSTIR	MTAP	MTOR	MUTYH	MYC	MYCL (MYCL1)	MYCN	MYD88
NBN	NF1	NF2	NFE2L2	NFKBIA	NKX2-1	NOTCH1	NOTCH2	NOTCH3
NPM1	NRAS	NT5C2	NTRK1	NTRK2	NTRK3	P2RY8	PALB2	PARK2
PARP1	PARP2	PARP3	PAX5	PBRM1	PDCD1 (PD-1)	PDCD1LG2 (PD-L2)	PDGFRA	PDGFRB
PDK1	PIK3C2B	PIK3C2G	PIK3CA	PIK3CB	PIK3R1	PIM1	PMS2	POLD1
POLE	PPARG	PPP2R1A	PPP2R2A	PRDM1	PRKAR1A	PRKCI	PTCH1	PTEN
PTPN11	PTPRO	QKI	RAC1	RAD21	RAD51	RAD51B	RAD51C	RAD51D
RAD52	RAD54L	RAF1	RARA	RB1	RBM10	REL	RET	RICTOR
RNF43	ROS1	RPTOR	SDHA	SDHB	SDHC	SDHD	SETD2	SF3B1
SGK1	SMAD2	SMAD4	SMARCA4	SMARCB1	SMO	SNCAIP	SOCS1	SOX2
SOX9	SPEN	SPOP	SRC	STAG2	STAT3	STK11	SUFU	SYK
TBX3	TEK	TET2	TGFBR2	TIPARP	TNFAIP3	TNFRSF14	TP53	TSC1
TSC2	TYRO3	U2AF1	VEGFA	VHL	WHSC1 (MMSET)	WHSC1L1	WT1	XPO1
XRCC2	ZNF217	ZNF703						

### Select Rearrangements<sup>2,3</sup>

Genes with select intronic regions for the detection of gene rearrangements, one gene with a promoter region and one non-coding RNA gene.

ALK	BCL2	BCR	BRAF	BRCA1	BRCA2	CD74	EGFR	ETV4
ETV5	ETV6	EWSR1	EZR	FGFR1	FGFR2	FGFR3	KIT	KMT2A (MLL)
MSH2	MYB	MYC	NOTCH2	NTRK1	NTRK2	NUTM1	PDGFRA	RAF1
RARA	RET	ROS1	RSPO2	SDC4	SLC34A2	TERC*	TERT† (PROMOTER ONLY)	TPR2

\* TERC is an ncRNA

† Promoter region of TERT is interrogated

FoundationOne<sup>®</sup>CDx is a qualitative next-generation sequencing based in vitro diagnostic test for advanced cancer patients with solid tumors and is for prescription use only. The test analyzes 324 genes as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) and is a companion diagnostic to identify patients who may benefit from treatment with specific therapies in accordance with the approved therapeutic product labeling. Additional genomic findings may be reported and are not prescriptive or conclusive for labeled use of any specific therapeutic product. Use of the test does not guarantee a patient will be matched to a treatment. A negative result does not rule out the presence of an alteration. Some patients may require a biopsy. For the complete label, including companion diagnostic indications and important risk information, please visit [www.FICDxLabel.com](http://www.FICDxLabel.com).

#### References:

1. Li M. Statistical Methods for Clinical Validation of Follow-On Companion Diagnostic Devices via an External Concordance Study. *Statistics in Biopharmaceutical Research* 8, 355-363 (2016).
2. Current as of January 2025. Please visit [www.foundationmedicine.com/ficdx](http://www.foundationmedicine.com/ficdx) for the most up-to-date gene list.
3. Refer to our full label for listing of intronic regions at <http://www.FICDxLabel.com>.



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