FOUNDATION MEDICINE®

Evidence Portfolio

FOUNDATIONONE®CDx

FOUNDATIONONE®LIQUID CDx

Non-Small Cell Lung Cancer (NSCLC)

FOUNDATIONONE®CDx

TUMOR TYPE	BIOMARKER(S) DETECTED	THERAPY	EVIDENCE	METHOD
Non-Small Cell Lung Cancer (NSCLC)	*EGFR* exon 19 deletions and *EGFR* exon 21 L858R alterations	EGFR Tyrosine Kinase Inhibitors (TKI) approved by FDA*	Iressa® (gefitinib). Prescribing Information. AstraZeneca Pharmaceuticals. 2021. Tagrisso® (osimertinib). Prescribing Information. AstraZeneca Pharmaceuticals. 2021. Tarceva® (erlotinib). Prescribing Information. Genentech USA, Inc. 2016.	Concordance with cobas® EGFR Mutation Test v2 (n = 282)
	EGFR exon 20 T790M alterations	Tagrisso® (osimertinib)	Tagrisso® (osimertinib). Prescribing Information. AstraZeneca Pharmaceuticals. 2021.	Concordance with cobas® EGFR Mutation Test v1 and cobas® EGFR Mutation Test v2 (n = 196)
	ALK rearrangements	Alecensa® (alectinib)	Alecensa® (alectinib). Genentech USA, Inc.; 2021.	Concordance with the FDA approved Ventana ALK CDx Assay and Vysis ALK Break-Apart FISH Probe Kit (n = 175), with samples from patients with histologically-confirmed NSCLC including enrolled patients as well as screen failures from the clinical trial NCT02075840, Roche study number BO28984 (also known as the ALEX study)
		Alunbrig® (brigatinib)	Alunbrig® (brigantinib). Prescribing Information. Takeda Pharmaceutical Company Limited. 2020.	
		Xalkori® (crizotinib)	Xalkori® (crizotinib). Prescribing Information. Pfizer Laboratories. 2021.	
		Zykadia® (ceritinib)	Zykadia® (ceritinib). Prescribing Information. Novartis Pharmaceuticals Corporation. 2019.	
	BRAF V600E	Braftovi® (encorafenib) in combination with Mektovi® (binimetinib)	BRAFTOVI. Prescribing Information. Array Biopharma Inc. 2023. Riely et al. J Clin Oncol. 2023; 41(21):3700-3711.	Retrospective confirmation of enrollment *BRAF* V600 mutations (originally detected by NGS or PCR) utilizing the FoundationOne®CDx assay (n=98)
	BRAF V600E	Tafinlar® (dabrafenib) in combination with Mekinist® (trametinib)	Tafinlar® (dabrafenib). Prescribing Information. Novartis Pharmaceuticals Corporation. 2021. Mekinist® (trametinib). Prescribing Information. Novartis Pharmaceuticals Corporation. 2021.	Concordance with cobas® 4800 BRAF V600 Mutation Test (n = 273, V600E samples only)
	MET single nucleotide variants (SNVs) and indels that lead to MET exon 14 skipping	Tabrecta® (capmatinib)	Tabrecta® (capmatinib). Package insert. Novartis Pharmaceuticals Corporation; 2020. Wolf, J. N Engl J Med. 2020:383(10):944-957. • Wolf J, et al. Journal of Thoracic Oncology. 2017; 12(11):S1578-S9. • Wolf J, et al. Annals of Oncology. 2018; 29:viii741-viii2.	Concordance between FoundationOne®CDx and enrollment clinical trial assay (RNA based RT-PCR) (n=198)
	ROS1 fusions	Rozlytrek® (entrectinib)	Rozlytrek® (entrectinib). Package insert. Genentech USA, Inc. 2023. Drilon A. Lancet Oncol. 2020:21(2):261-270.	Clinical bridging study utilizing samples from patients with *ROS1* fusions enrolled in three clinical trials (ALKA, STARTRK-1, and STARTRK-2) which supported the FDA-approval of entrectinib for adult patients with metastatic NSCLC whose tumors are ROS1-positive

*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
The indications for use of FoundationOne®CDx, including all FDA-approved companion diagnostic claims can be found at: http://www.f1cdxlabel.com/
Milbury CA, et al. (2022) Clinical and analytical validation of FoundationOne®CDx, a comprehensive genomic profiling assay for solid tumors. PLoS ONE 17(3): e0264138.

TUMOR TYPE	BIOMARKER(S) DETECTED	THERAPY	EVIDENCE	METHOD
Melanoma	*BRAF* V600E	BRAF Inhibitors approved by FDA*	BRAFTOVI. Prescribing information. Array Biopharma Inc; 2020. MEKTOVI. Prescribing information. Array Biopharma Inc; 2020. TAFINLAR. Prescribing information. Novartis Pharmaceuticals Corporation; 2021. Boussemart, L. Oncologist. 2019:24(5):657-663.	Concordance with cobas® 4800 BRAF V600 Mutation Test[a]
	BRAF V600E and V600K	Mekinist® (trametinib) or BRAF/MEK Inhibitor Combinations approved by FDA*	MEKINIST. Prescribing information. Novartis Pharmaceuticals Corporation; 2021. Boussemart, L. Oncologist. 2019:24(5):657-663.	Concordance with cobas® 4800 BRAF V600 Mutation Test
	BRAF V600 mutation-positive	Tecentriq® (atezolizumab) in combination with Cotellic® (cobimetinib) and Zelboraf® (vemurafenib)	TECENTRIQ. Prescribing information. Genentech USA, Inc; 2021. COTELLIC. Prescribing information. Genentech USA, Inc.; 2018. ZELBORAF. Prescribing information. Genentech USA, Inc.; 2020. Boussemart, L. Oncologist. 2019:24(5):657-663.	Study using the THxIDTM 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
Breast Cancer	*ERBB2* (HER2) amplification	Herceptin® (trastuzumab), Kadcyla® (ado-trastuzumab-emtansine), or Perjeta® (pertuzumab)	Herceptin® (trastuzumab). Package insert. Genentech USA, Inc. 2010. Kadcyla® (ado-trastuzumab-emtansine). Package insert. Genentech USA, Inc. 2013. Perjeta® (pertuzumab). Package insert. Genentech USA, Inc. 2012.	Comparator assay with HER2 FISH PharmDx1 Kit (Dako Denmark, A/S)
	PIK3CA C420R, E542K, E545A, E545D [1635G>T only], E545G, E545K, Q546E, Q546R, H1047L, H1047R, and H1047Y alterations	Piqray® (alpelisib)	Piqray® (alpelisib). Package insert. Novartis Pharmaceuticals Corporation. 2019. Andre F, et al. N Engl J Med. 2019; 380(20):1929-1940.	Clinical bridging via concordance to clinical trial assays (CTAs) using samples from SOLAR-1
	AKT1 E17K; *PIK3CA* R88Q, N345K, C420R, E542K, E545A, E545D, E545Q, E545K, E545G, Q546E, Q546K, Q546R, Q546P, M1043V, M1043I, H1047Y, H1047R, H1047L, and G1049R; and *PTEN* alterations	Truqap™ (capivasertib) in combination with Faslodex® (fulvestrant)	Turner, NC et al. N Engl J Med. 2023: 388(22):2058-2070. TRUQAP™ (capivasertib). Prescribing information. AstraZeneca 2023.	FoundationOne®CDx used as the clinical trial assay in CAPItello-291 (NCT04305496), a randomized, phase 3 double-blind trial of capivasertib plus fulvestrant versus placebo plus fulvestrant in patients with hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer who had had a relapse or disease progression during or after treatment with an aromatase inhibitor.

[a]Sensitivity of dinucleotide detection of BRAF V600K and V600E was found to be significantly reduced in cobas® BRAF test, for samples in which FoundationOne®CDx detected the dinucleotides to be of lower than 40% MAF, leading to low NPA values.
*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
Milbury CA, et al. (2022) Clinical and analytical validation of FoundationOne®CDx, a comprehensive genomic profiling assay for solid tumors. PLoS ONE 17(3): e0264138.
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TUMOR TYPE	BIOMARKER(S) DETECTED	THERAPY	EVIDENCE	METHOD
Colorectal Cancer	*KRAS* wild-type (absence of mutations in codons 12 and 13)	Erbitux® (cetuximab)	Erbitux® (cetuximab). Package insert. Bristol-Myers Squibb Company. 2012.	Concordance with therascreen® KRAS RGQ PCR Kit (QIAGEN)
	KRAS wild-type (absence of mutations in exons 2, 3, and 4) and NRAS wild type (absence of mutations in exons 2, 3, and 4)	Vectibix® (panitumumab)	Vectibix® (panitumumab). Package insert. Amgen Inc. 2009.	Concordance with clinical trial assay, therascreen® KRAS RGQ PCR Kit (QIAGEN)
Ovarian Cancer	*BRCA1/2* alterations	Lynparza® (olaparib)	Lynparza® (Olaparib). Package insert. AstraZeneca: 2020.	FoundationOne®CDx used as a clinical trial assay in the SOLO1 trial (D0818C0001) for olaparib
Cholangiocarcinoma	*FGFR2* fusions and select rearrangements	Pemazyre® (pemigatinib)	Pemazyre® (pemigatinib). Package insert. Incyte Corporation. 2022. Abou-Alfa GK, et al. The Lancet Oncology. 2020; 21(5):671–84.	Clinical bridging via concordance to clinical trial assays (CTAs) using samples from FIGHT-202 and CBGJ398X2204
Prostate Cancer	Homologous Recombination Repair (HRR) gene *(BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D* and *RAD54L)* alterations	Lynparza® (olaparib)	Lynparza® (Olaparib). Package insert. AstraZeneca: 2020. de Bono J. N Engl J Med. 2020:382(22):2091-2102.	FoundationOne®CDx clinical trial assay in PROfound trial (NCT02987543), outcomes analysis performed with samples confirmed to be positive via FDA version of FoundationOne®CDx.
	BRCA1/2 alterations	AKEEGA™ (niraparib and abiraterone acetate)	AKEEGA™ Package insert. Janssen:2023.	FoundationOne®CDx clinical trial assay in MAGNITUDE trial (NCT03748641), outcomes analysis performed with samples confirmed to be positive via FDA version of FoundationOne®CDx, see section 14.1 AKEEGA package insert.
	BRCA1/2 alterations	Lynparza® (olaparib) in combination with abiraterone	Saad et al. Lancet Oncology. 2023; 24(10):1094-108.	FoundationOne®CDx used as the clinical trial assay in PROpel (NCT03732820), a double-blind, randomized phase 3 trial of abiraterone and olaparib versus abiraterone and placebo in first-line treatment of patients with mCRPC.

Milbury CA, et al. (2022) Clinical and analytical validation of FoundationOne®CDx, a comprehensive genomic profiling assay for solid tumors. PLoS ONE 17(3): e0264138.
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TUMOR TYPE	BIOMARKER(S) DETECTED	THERAPY	EVIDENCE	METHOD
Solid Tumors	MSI-High	Keytruda® (pembrolizumab)	Keytruda® (pembrolizumab). Package insert. Merck & Co.: 2023.	Clinical bridging study utilizing samples from patients with MSI-H solid tumors enrolled in two clinical trials (KEYNOTE-158 Cohort K, KEYNOTE-164) which provided data supporting the FDA-approval of pembrolizumab for MSI-H patients across all solid tumor types. KEYNOTE-158 Cohort K is a multicenter, non-randomized, open-label trial of pembrolizumab in participants with unresectable or metastatic MSI-H/dMMR solid tumors (except CRC) that have progressed following prior treatment and who have no satisfactory alternative treatment options. KEYNOTE-164 is a multicenter, non-randomized, open-label trial designed to evaluate the efficacy of pembrolizumab in previously treated participants with unresectable or metastatic MSI-H/dMMR CRC tumors. In the clinical trials, MSI-H status was prospectively determined for enrollment based on local IHC testing or PCR assays (clinical trial assays).
	TMB ≥ 10 mutations per megabase	Keytruda® (pembrolizumab)	Keytruda® (pembrolizumab). Package insert. Merck & Co.: 2023. Marabelle A, et al. Lancet Oncol. 2020 Oct;21(10):1353-1365. Marcus L, et al. Clin Cancer Res. 2021 Sep 1;27(17):4685-4689.	In KEYNOTE-158 tissue TMB (tTMB) was assessed in formalin-fixed paraffin-embedded tumour samples using the FoundationOne®CDx assay. The prespecified definition of tTMB-high status was at least 10 mutations per megabase.
	NTRK1/2/3 fusions	Rozlytrek® (entrectinib)	Rozlytrek® (entrectinib). Package insert. Genentech USA, Inc.: 2023. Drilon A. N Engl J Med. 2018;378(8):731–739.	Clinical validity and clinical utility of FoundationOne®CDx for this indication is provided in section 10.8 of the FDA label (http://f1lcdxlabel.com/), *Clinical Bridging Study: Detection of NTRK1/2/3 Fusions to Determine Eligibility for Treatment with Entrectinib*
		Vitrakvi® (larotrectinib)	Vitrakvi® (larotrectinib). Package insert. Bayer HealthCare Pharmaceuticals Inc. 2021. Drilon A. N Engl J Med. 2018;378(8):731–739. Hong DS, et al. The Lancet Oncology. 2020; 21(4):531–40.	Clinical bridging via concordance to clinical trial assays (CTAs)* using samples from LOXO-TRK-14001, NAVIGATE, and SCOUT and supplemental *NTRK* fusion negative samples (n=270 for concordance)
	RET fusions	Retevmo® (selpercatinib)	Subbiah et al. The Lancet Oncology. 2022; 23(10):1261-1273. Duke et al. Clin Cancer Res. 2023; 29(18):3573-3578.	Clinical bridging via concordance of FoundationOne®CDx to the CTAs using available patient samples from the LIBRETTO-001 clinical study (N = 175) and the supplemental RET fusion negative samples (N = 311). The clinical validity and utility of FoundationOne®CDx for the detection of RET fusions in patients with solid tumors was based on estimation of clinical efficacy (ORR) in the F1CDx-positive population and subgroups of the CTA+ population by FoundationOne®CDx status.

Milbury CA, et al. (2022) Clinical and analytical validation of FoundationOne®CDx, a comprehensive genomic profiling assay for solid tumors. PLoS ONE 17(3): e0264138.
The indications for use of FoundationOne®CDx, including all FDA-approved companion diagnostic claims can be found at: http://www.f1cdxlabel.com/
*Based on Foundation Medicine, Memorial Sloan Kettering Cancer Center, and University of Washington CGP assays

Non-Small Cell Lung Cancer (NSCLC) Companion Diagnostic Indications[1]

FOUNDATIONONE® LIQUID CDx

TUMOR TYPE	BIOMARKER(S) DETECTED	THERAPY	EVIDENCE	METHOD
Non-Small Cell Lung Cancer (NSCLC)	*ALK* rearrangements	ALECENSA® (alectinib)	Dziadziuszko R. J Thorac Oncol. July 24, 2021. Peters S. N Engl J Med. 2017:377(9):829-838. Camidge DR. Journal of Thoracic Oncology 14.7 (2019): 1233-1243.	Clinical bridging via concordance to Foundation Medicine clinical trial assay (CTA), FoundationACT liquid biopsy from BFAST Cohort A (n=262), see section 10.1 in the FoundationOne®Liquid CDx label[1]
	EGFR exon 19 deletions and EGFR exon 21 L858R substitution	EGFR Tyrosine Kinase Inhibitors (TKI) approved by FDA	Lee CK. J Natl Cancer Inst. 2017:109(6):djw279. Yi L. Int J Cancer. 2019:145(1):284-294. Husain H, et al. JCO Precision Oncology no. 6 (2022) e2200261. Schwartzberg LS, et al. Journal of Clinical Oncology 40, no. 16_suppl (June 01, 2022) e18778-e18778.	FoundationOne®Liquid CDx concordance study to cobas® EGFR Mutation Test v2 for EGFR exon 19 deletion and EGFR exon 21 L858R alteration, see section 10.2 n the FoundationOne®Liquid CDx label[1]
	MET single nucleotide variants (SNVs) and indels that lead to MET exon 14 skipping	TABRECTA® (capmatinib)	Wolf, J. N Engl J Med. 2020:383(10):944-957.	Clinical bridging via concordance to tissue-based clinical trial assay (RT-PCR) using samples from GEOMETRY mono-1 (n=150)* see section 10.6 in the FoundationOne®Liquid CDx label[1]
	ROS1 fusions**	ROZLYTREK® (entrectinib)	Drilon A, Lancet Oncol. 2020;21(2):261-270 Dziadziuszko R, et al. Mol Oncol. 2022 May; 16(10):2000-2014.	Clinical bridging study via concordance to the CTAs for the STARTRK-2 clinical trial (n=175)* see section 10.7 in the FoundationOne®Liquid CDx label[1]
	BRAF V600E	Braftovi® (encorafenib) in combination with Mektovi® (binimetinib)	BRAFTOVI. Prescribing Information. Array Biopharma Inc. 2023.	Clinical bridging study via concordance to the CTAs in the PHAROS study (n = 81).

1. FoundationOne Liquid CDx. Technical Information. Foundation Medicine, Inc; 2024. http://www.f1cdxlabel.com/
2. Woodhouse R, Li M, Hughes J, et al. Clinical and analytical validation of FoundationOne Liquid CDx, a novel 324-Gene cfDNA-based comprehensive genomic profiling assay for cancers of solid tumor origin. PLoS One. 2020;15(9):e0237802. Published 2020 Sep 25. doi:10.1371/journal.pone.0237802.

*Data represents samples with ≥30 ng cfDNA input
**When tissue is unavailable.

Note that clinical bridging studies typically include concordance studies to the clinical trial assays (Foundation Medicine or other) and efficacy analysis including the companion diagnostic data for the FDA-approved CDx.

Prostate Cancer, Breast Cancer, Colorectal Cancer and Solid Tumors Companion Diagnostic Indications[1]

FOUNDATIONONE®LIQUID CDx

TUMOR TYPE	BIOMARKER(S) DETECTED	THERAPY	EVIDENCE	METHOD
Prostate Cancer	*BRCA1, BRCA2, ATM* alterations	LYNPARZA® (olaparib)	de Bono J. N Engl J Med. 2020:382(22):2091-2102.	Clinical bridging via concordance to the FoundationOne®CDx-based clinical trial assay (CTA) for the PROfound trial (n=245), see section 10.3 in the FoundationOne®Liquid CDx label[1]
	BRCA1/2 alterations	AKEEGA® (niraparib + abiraterone acetate)	FoundationOne®Liquid CDx Technical Label. RAL-0035-12.	The clinical performance of FoundationOne®Liquid CDx in detecting *BRCA1* and *BRCA2* alterations in patients with PC who may benefit from treatment with AKEEGA was established by clinically bridging the drug efficacy of patients enrolled in MAGNITUDE clinical trial by the plasma-based Clinical Trial Assay (CTA) to the patient population selected by FoundationOne®Liquid CDx.
	BRCA1/2 alterations	RUBRACA® (rucaparib)	Abida W. J Clin Oncol. 2020:38(32):3763-3772.	Clinical bridging via concordance to the CTAs (including FoundationOne, FoundationOne®Liquid and local testing) using pre-treatment samples from TRITON2 (n=209), see section 10.4 in the FoundationOne®Liquid CDx label[1]
	BRCA1/2 alterations	Lynparza® (olaparib) in combination with abiraterone and prednisone or prednisolone	Saad et al. Lancet Oncology. 2023; 24(10):1094-108.	FoundationOne®Liquid CDx used as the clinical trial assay in PROpel (NCT03732820), a double-blind, randomized phase 3 trial of abiraterone and olaparib versus abiraterone and placebo in first-line treatment of patients with mCRPC.
Breast Cancer	*PIK3CA* mutations C420R, E542K, E545A, E545D [1635G>T only], E545G, E545K, Q546E, Q546R; and H1047L, H1047R, and H1047Y	PIQRAY® (alpelisib)	André F. N Engl J Med. 2019:380(20): 1929-1940. Woodhouse R. PLoS One. 2020;15(9):e0237802 (see section on PIK3CA)	Clinical bridging via concordance to CTA based on tumor tissue polymerase chain reaction (PCR) using pre-treatment samples and evaluable analysis from the SOLAR-1 trial (n=359). See Woodhouse et al. and section 10.5 in the FoundationOne®Liquid CDx label[1]
Solid Tumors	*NTRK1/2/3* fusions*	ROZLYTREK® (entrectinib)	Dziadziuszko R, et al. Mol Oncol. 2022 May; 16(10):2000-2014. Doebele RC, et al. Lancet Oncol. 2020 Feb;21(2):271-282.	Clinical Bridging Study via concordance to the CTAs for the STARTRK-2 clinical trial (n=256), see section 10.8 of the FDA label for FoundationOne®Liquid CDx)
Colorectal Cancer (CRC)	*BRAF* V600E	BRAFTOVI® (encorafenib) in combination with cetuximab	Kopetz S, et al. N Engl J Med. 2019;381(17):1632-1643.	Clinical bridging study via concordance to the tissue-based clinical trial assay for the BEACON trial (n=433), see section 10.10 in the FoundationOne®Liquid CDx label[1]

1. FoundationOne Liquid CDx. Technical Information. Foundation Medicine, Inc; 2024. http://www.f1cdxlabel.com/
2. Woodhouse R, Li M, Hughes J, et al. Clinical and analytical validation of FoundationOne Liquid CDx, a novel 324-Gene cfDNA-based comprehensive genomic profiling assay for cancers of solid tumor origin. PLoS One. 2020;15(9):e0237802. Published 2020 Sep 25. doi:10.1371/journal.pone.0237802.

*When tissue is unavailable.

Note that clinical bridging studies typically include concordance studies to the clinical trial assays (Foundation Medicine or other) and efficacy analysis including the companion diagnostic data for the FDA-approved CDx.

FOUNDATION MEDICINE®

FoundationOne®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.F1CDxLabel.com

FoundationOne®Liquid CDx is for prescription use only and is a qualitative next-generation sequencing based in vitro diagnostic test for advanced cancer patients with solid tumors. The test analyzes 324 genes utilizing circulating cell-free DNA and is FDA-approved to report short variants in 311 genes and as a companion diagnostic to identify patients who may benefit from treatment with specific therapies (listed in Table 1 of the Intended Use) 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. Patients being considered for eligibility for therapy based on detection of *NTRK1/2/3* and *ROS1* fusions should only be tested if tissue is unavailable. Patients who are negative for other companion diagnostic mutations should be reflexed to tumor tissue testing and mutation status confirmed using an FDA-approved tumor tissue test, if feasible. For the complete label, including companion diagnostic indications and complete risk information, please visit www.F1LCDxLabel.com.

For the complete label, including companion diagnostic indications and important risk information, please visit www.F1CDxLabel.com and www.F1LCDxLabel.com.