FOUNDATIONONE CDx™

Transform genomic data into real-life results

FoundationOne CDx™ is the next evolution of FoundationOne® with a clinically and analytically validated NGS platform to empower your clinical decision support to oncologists

New **FDA-Approved** Broad Companion Diagnostic (CDx) for Solid Tumors with Medicare Coverage[1]

FDA Approved. Clinically Validated.

- **Clinical Validation**: Proven concordance with multiple companion diagnostics and approved by the FDA for any solid tumor based on clinical and analytical validation of over 6,300 samples[2]
- **Comprehensive Results**: Evaluates genomic alterations, including base substitutions, insertions and deletions, copy number alterations and fusions or rearrangements, as well as genomic signatures, such as microsatellite instability (MSI) and tumor mutational burden (TMB), with uniform and deep sequencing on the Illumina® HiSeq 4000
- **Coverage**: National coverage for qualifying Medicare and Medicare Advantage patients across all solid tumors[1]

Summary of Clinical Concordance 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).[3] All studies passed the acceptance criteria specified in each study protocol.

BIOMARKER	POSITIVE-PERCENT AGREEMENT (PPA)[4]	NEGATIVE-PERCENT AGREEMENT (NPA)	COMPARATOR METHOD[5]
EGFR Exon 19 Deletions and L858R	**98.1%** (106/108)	**99.4%** (153/154)	cobas® *EGFR* Mutation Test v2
EGFR T790M	**98.9%** (87/88)	**86.1%** (93/108)	cobas® *EGFR* Mutation Test v1 cobas® *EGFR* Mutation Test v2
ALK Rearrangements	**92.9%** (78/84)	**100%** (75/75)	Ventana *ALK* (D5F3) CDx Assay Vysis *ALK* Break-Apart FISH Probe Kit
KRAS	**100%** (173/173)	**100%** (154/154)	therascreen® *KRAS* RGQ PCR Kit
ERBB2 (HER2) Amplifications	**89.4%** (101/113)	**98.4%** (180/183)	Dako HER2 FISH PharmDx® Kit
BRAF V600 *BRAF* V600E	**99.4%** (166/167) **99.3%** (149/150)	**89.6%** (121/135)[6] **99.2%** (121/122)	cobas® *BRAF* V600 Mutation Test
BRAF V600 dinucleotide[7]	**96.3%** (26/27)	**100%** (24/24)	THxID® *BRAF* kit

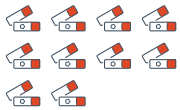
Cobas® is a trademark of Roche Diagnostics Operations, Inc. Therascreen® is a trademark of Qiagen. PharmDx® is a registered trademark of Dako Denmark A/S.

Saves Time and Tissue

- Spares tissue compared with sequential single-gene tests—All FoundationOne CDx™ results are provided from one FFPE block or a 10-slide sample with H&E slide[8]
- No equipment purchase required
- Samples are sent to our lab and analyzed by Foundation Medicine's team of genomic scientists, pathologists, and computational biologists
- Comprehensive platform that can be updated regularly as more genes and genomic signatures are indicated for use with FDA-approved therapies

Tissue Needed

(Example in NSCLC)

FoundationOne CDx*	TRADITIONAL TESTING	NUMBER OF SLIDES
 **10 Slides or 1 FFPE Block (+H&E Slide)**	PD-L1	2–4 Slides
	EGFR Mutations	2–4 Slides
	ALK Rearrangements	2–4 Slides
	ROS1 Rearrangements[9,10]	2–4 Slides
	After the fourth driver is tested, almost 50% patients will have run out of tissue[9,10]	
	BRAF V600E Mutations	2–4 Slides
	MET Mutations	2–4 Slides
	RET Rearrangements	2–4 Slides
	ERBB2 Amplifications	2–4 Slides
	KRAS Mutations	2–4 Slides
	TOTAL	18–36 Slides

*PD-L1 by Immunohistochemistry (IHC) can be ordered as an additional test with 2-4 slides of tissue needed.

No "14-Day Rule" for Outpatients Tested with Foundation Medicine® Tests[11]

- Centers for Medicare and Medicaid Services (CMS) issued changes to the Hospital Outpatient Prospective Payment System (HOPPS) Final Rule, also known as the "14-Day Rule" to establish a new exception to CMS date of service policy effective Jan. 1, 2018
- The new policy eliminates the "14-Day Rule" for molecular pathology tests when the test is performed on a specimen collected during an outpatient visit
- The new rule applies to DNA and RNA molecular pathology tests—IHC tests are not excluded from the new rule and Foundation Medicine is required to continue to bill facilities for these cases ordered within 14 days from the outpatient or inpatient discharge
- For full details on the "14-Day Rule", visit **www.foundationmedicine.com/pages/medicare-compliance**

TO LEARN MORE:

Visit www.foundationmedicine.com/f1cdx

TO ORDER:

Create an account to order online at www.foundationmedicine.com/signup

References

1. Medicare and Medicare Advantage members have coverage of FoundationOne CDx in accordance with the Centers for Medicare and Medicaid Services (CMS) national coverage determination (NCD) criteria. **2.** Samples and cell lines in clinical and analytical validation for FoundationOne CDx. See the following link for complete summary of safety and efficacy data by the FDA: *www.foundationmedicine.com/f1cdx.* **3.** 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). **4.** 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. **5.** Follow-on CDx claims were based on a non-inferiority statistical testing approach using the enrichment design presented by Li M. Statistical Methods for Clinical Validation of Follow-On Companion Diagnostic Devices via an External Concordance Study. Statistics in Biopharmaceutical Research. Volume 8, 2017 – Issue 3: pages 355–363. **6.** 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. **7.** A study using the THxID® BRAF kit (bioMérieux) was conducted with samples with BRAF V600 dinucleotide mutation detected by F1CDx and BRAF V600 negative samples to provide a better evaluation of V600 dinucleotide concordance. **8.** Results can vary based on percent tumor nuclei within the tissue sample. For best results, please follow our specimen instructions. **9.** Ali SM, et al. Comprehensive genomic profiling identifies a subset of crizotinib-responsive ALK-rearranged non-small cell lung cancer not detected by FISH. *The Oncologist.* 2016 Jun;21(6):762–770. **10.** Schrock AB, et al. Comprehensive genomic profiling identifies frequent drug-sensitive EGFR exon 19 deletions in NSCLC not identified by prior molecular testing. *Clin Cancer Res.* 2016 Jul;22(13):3281–5. **11.** As a molecular pathology test, FoundationOne CDx™ should fall within the new exception to the date of service policy regardless of ADLT status. Following assignment of a Proprietary Laboratory Analyses (PLA) code for FoundationOne CDx, we will confirm with Centers for Medicare and Medicaid Services (CMS) that the new code is status indicator "A", and excluded from the outpatient packaging policy.

FoundationOne CDx™ is a next-generation sequencing based *in vitro* diagnostic device for detection of substitutions, insertion and deletion alterations, and copy number alterations 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. For the complete intended use statement, including companion diagnostic indications, please see the FoundationOne CDx Technical Information, *www.foundationmedicine.com/f1cdx.*

FOUNDATION MEDICINE®