FOUNDATION MEDICINE®

FoundationOne®Liquid CDx
Patient Report Guide

FoundationOne Liquid CDx is a liquid biopsy test, ordered by your doctor, that looks for mutations and biomarkers in your cancer's DNA, using your blood sample. The results of this test can help you and your doctor decide together on the next best step in your treatment plan. This report guide can help prepare you to review and discuss your test results with your doctor.

How to use this guide:

- Use this guide *after* your results are ready.
- You can request a copy of your FoundationOne Liquid CDx report by contacting our Client Services team at 888-988-3639 or emailing client.services@foundationmedicine.com.
- This guide will walk you through each section, focusing on the first two pages of your report, with numbers to call out different parts of the report.
- The report images in this guide are from a sample report, which can help you read your actual report. This guide does not contain your actual report. Your report may have a different length of pages from the sample report, which may cause some sections of your report to land on different pages from the sample report.
- A **GLOSSARY** of key terms is included on the last page of this guide.

Report Page One

The first page of your report contains a summary of the gene mutations and biomarkers found by testing your sample.

1

Biomarker Findings

Microsatellite instability (MSI) and tumor mutational burden (TMB) are two biomarkers that can help your doctor understand what immunotherapy treatment options might be available for you.

2

Genomic Findings

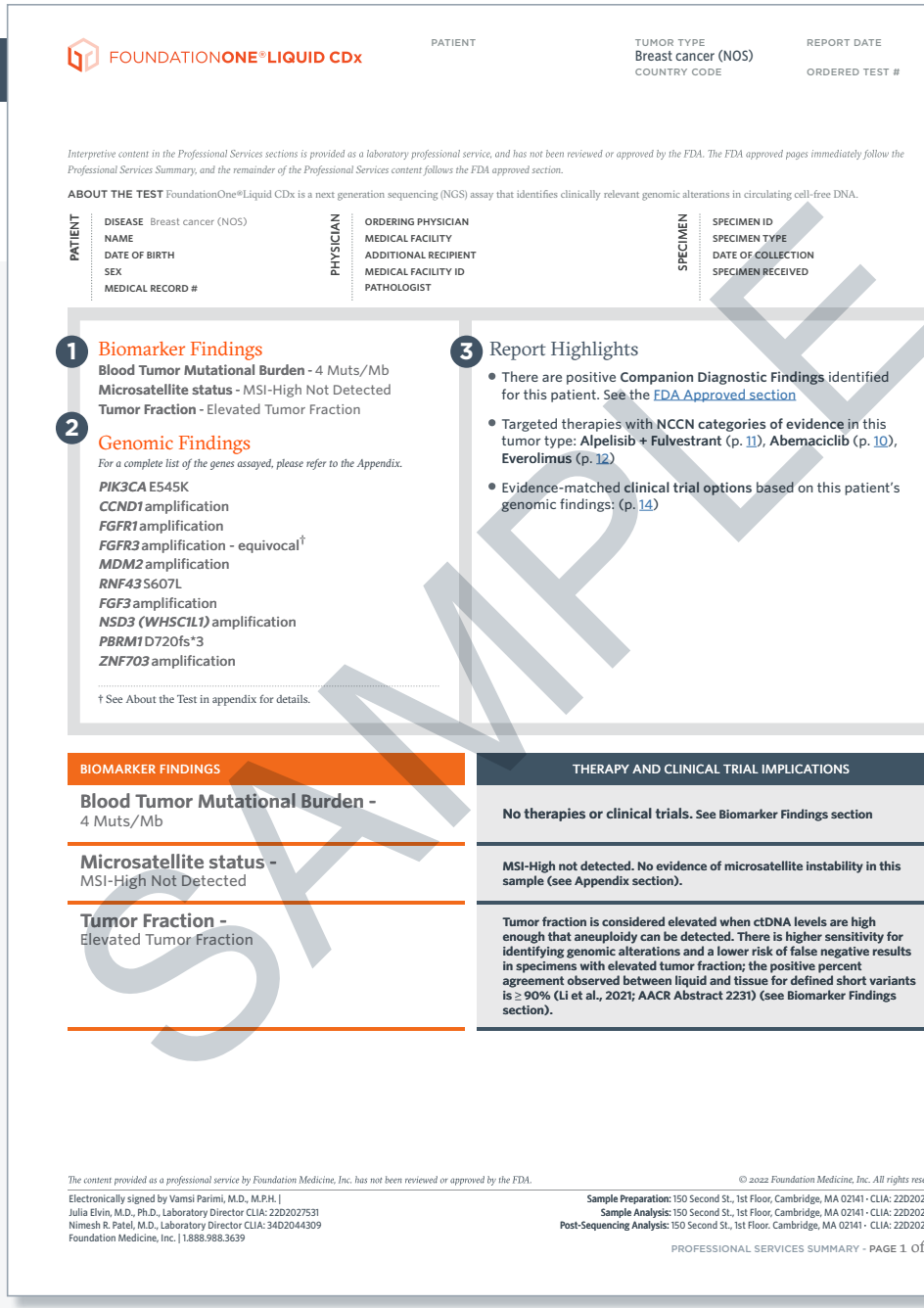
This section shows the gene mutations that may be linked with treatment options. This includes the names of genes where a mutation was found (e.g., "*PIK3CA*") along with a description of that mutation (e.g., "E545k").

3

Report Highlights

This provides the highlights from your results, at a glance, to help your doctor focus on the key actionable results for treatment planning.

If your report mentions that you have positive companion diagnostic (CDx) findings, these are described in more detail in the later pages of the report. This refers to an additional layer of results. However, all of your test findings and treatment options are described in the first summary section.



FOUNDATIONONE®LIQUID CDx

PATIENT

TUMOR TYPE
Breast cancer (NOS)
COUNTRY CODE

REPORT DATE

ORDERED TEST #

Interpretive content in the Professional Services sections is provided as a laboratory professional service, and has not been reviewed or approved by the FDA. The FDA approved pages immediately follow the Professional Services Summary, and the remainder of the Professional Services content follows the FDA approved section.

ABOUT THE TEST FoundationOne®Liquid CDx is a next generation sequencing (NGS) assay that identifies clinically relevant genomic alterations in circulating cell-free DNA.

PATIENT
DISEASE Breast cancer (NOS)
NAME
DATE OF BIRTH
SEX
MEDICAL RECORD #

PHYSICIAN
ORDERING PHYSICIAN
MEDICAL FACILITY
ADDITIONAL RECIPIENT
MEDICAL FACILITY ID
PATHOLOGIST

SPECIMEN
SPECIMEN ID
SPECIMEN TYPE
DATE OF COLLECTION
SPECIMEN RECEIVED

1 Biomarker Findings

Blood Tumor Mutational Burden - 4 Muts/Mb
Microsatellite status - MSI-High Not Detected
Tumor Fraction - Elevated Tumor Fraction

2 Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

PIK3CA E545K
CCND1 amplification
FGFR1 amplification
FGFR3 amplification - equivocal†
MDM2 amplification
RNF43 S607L
FGF3 amplification
NSD3 (WHSC1L1) amplification
PBRM1 D720fs*3
ZNF703 amplification

† See About the Test in appendix for details.

3 Report Highlights

- There are positive **Companion Diagnostic Findings** identified for this patient. See the FDA Approved section
- Targeted therapies with **NCCN categories of evidence** in this tumor type: **Alpelisib + Fulvestrant** (p. 11), **Abemaciclib** (p. 10), **Everolimus** (p. 12)
- Evidence-matched **clinical trial options** based on this patient's genomic findings: (p. 14)

BIOMARKER FINDINGS	THERAPY AND CLINICAL TRIAL IMPLICATIONS
Blood Tumor Mutational Burden - 4 Muts/Mb	**No therapies or clinical trials.** See Biomarker Findings section
Microsatellite status - MSI-High Not Detected	**MSI-High not detected. No evidence of microsatellite instability in this sample (see Appendix section).**
Tumor Fraction - Elevated Tumor Fraction	**Tumor fraction is considered elevated when ctDNA levels are high enough that aneuploidy can be detected. There is higher sensitivity for identifying genomic alterations and a lower risk of false negative results in specimens with elevated tumor fraction; the positive percent agreement observed between liquid and tissue for defined short variants is ≥ 90% (Li et al., 2021; AACR Abstract 2231) (see Biomarker Findings section).**

SAMPLE

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PROFESSIONAL SERVICES SUMMARY - PAGE 1 of

Report Page Two

4 Therapies with Clinical Relevance

These are potential treatment options based on your genomic findings.

The therapies listed in the left column are FDA-approved for your cancer type. The therapies in the right column are FDA-approved for another cancer type. You and your doctor can discuss if any of these treatments may be right for you.

5 Clinical Trial Options

Your results may match with treatments that are currently being developed in clinical trials. A clinical trial could help you access some of the newest treatments in development. Talk to your doctor about available clinical trials you might qualify for.

What if there are no treatment options listed in my report?

Even if the results do not identify a specific therapy or clinical trial for you, they can still provide valuable information to you and your doctor. They may identify treatments that are not appropriate for you based on your genomic findings, they may confirm your current treatment, or they may be useful in the future as additional treatments become available.

FOUNDATIONONE®LIQUID CDx

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4

GENOMIC FINDINGS		VAF%	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
PIK3CA -	E545K	0.65%	Alpelisib + Fulvestrant 1	Everolimus 2A
				Temsirolimus
10 Trials see p. 21				
CCND1 -	amplification	-	Abemaciclib 2A	None
10 Trials see p. 14				
FGFR1 -	amplification	-	None	Pazopanib
10 Trials see p. 16				
FGFR3 -	amplification - equivocal	-	None	None
10 Trials see p. 18				
MDM2 -	amplification	-	None	None
5 Trials see p. 20				
RNF43 -	S607L	0.58%	None	None
3 Trials see p. 23				

5

NCCN category

GENOMIC FINDINGS WITH NO REPORTABLE THERAPEUTIC OR CLINICAL TRIAL OPTIONS

For more information regarding biological and clinical significance, including prognostic, diagnostic, germline, and potential chemosensitivity implications, see the Genomic Findings section.

FGF3 - amplification p. 8
NSD3 (WHSC1L1) - amplification p. 8
PBRM1 - D720fs*3 p. 9
ZNF703 - amplification p. 9

IMPORTANT NOTE Genomic alterations detected may be associated with activity of certain FDA-approved drugs, however, the agents listed in this report may have varied clinical evidence in the patient's tumor type. Nei the therapeutic agents nor the clinical trials identified are ranked in order of potential or predicted efficacy for this patient, nor are they ranked in order of level of evidence for this patient's tumor type. In the appropriate clinical context, germline testing of *APC; ATM; BAP1; BRCA1; BRCA2; BRIP1; CHEK2; FH; FLCN; MEN1; MLH1; MSH2; MSH6; MUTYH; NF1; NF2; PALB2; PMS2; POLE; PTEN; RAD51C; RAD51D; RB1; RET; SDHA; SDHB; SDHC; SDH SMAD4; STK11; TGFBR2; TP53; TSC1; TSC2; VHL*, and *WT1* is recommended.

Variant Allele Frequency is not applicable for copy number alterations.

SAMPLE

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PROFESSIONAL SERVICES SUMMARY - PAGE 2 of

The Rest of the Report

This report guide is focused only on the first few pages of your report to help you understand the summary of your genomic and biomarker findings and the treatment options that may be available to you. Your full report contains additional pages with detailed information that your doctor may use to better understand your findings. The FoundationOne Liquid CDx test is an FDA-approved companion diagnostic for corresponding FDA-approved therapies. Any CDx-associated findings can be found on the FDA-approved page of your report, which follows the initial pages described in this report guide. Read on to see a glossary of key terms discussed in the guide.

Key Terms

Alterations
Changes in the DNA that can influence cancer growth (also called "mutations").

Biomarker
A marker found in blood or tissues that may provide your doctor with information about potential treatment options. For example, the status of certain biomarkers can predict response to immunotherapy.

Biomarker Findings
On your FoundationOne Liquid CDx report, the "Biomarker Findings" section includes the following biomarkers: microsatellite instability (MSI) and blood tumor mutational burden (bTMB). A high level of either of these two biomarkers may indicate that you could benefit from immunotherapy. Please note, however, that in other contexts, "biomarkers" may also include gene mutations.

Biomarker Testing
You may also hear the testing referred to as genomic testing, tumor testing, molecular testing, next-generation sequencing (NGS), and genomic profiling. Biomarker testing is a general category of testing that looks for mutations in cancer genes to identify potential treatment options. Foundation Medicine performs a type of biomarker testing called comprehensive genomic profiling (CGP).

Blood Tumor Mutational Burden (bTMB)
A biomarker that can be detected from your blood sample and that may help predict response to immunotherapy. bTMB is a measure of the frequency of mutations in your circulating-tumor DNA (ctDNA) when performing FoundationOne Liquid CDx.

Cells
Basic units that make up your body.

Circulating-tumor DNA (ctDNA)
Small DNA fragments that have come from your tumor and can be found circulating in your blood.

Clinical Trial
A type of research study that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis, or treatment of a disease.

Companion Diagnostic (CDx)
A medical device which provides information essential for the safe and effective use of a corresponding therapy. The test helps doctors determine if a particular treatment's benefits to a patient will outweigh any potential risks.

Comprehensive Genomic Profiling (CGP)
A method of cancer testing that can find the mutations in your DNA that may be causing your cancer to grow. This is the type of testing performed by Foundation Medicine.

DNA
The molecules inside cells that carry genetic information and pass it from one generation to the next. DNA instructs cells how to grow and divide; DNA mutations may lead to cancer growth.

Food and Drug Administration (FDA)
The official US government agency responsible for review and approval of drugs and certain diagnostic tests to determine their safety and effectiveness for the intended use in patients.

Foundation Medicine
Company that performs biomarker/genomic testing called comprehensive genomic profiling (CGP).

FoundationOne Liquid CDx
A next-generation sequencing test developed by Foundation Medicine that analyzes over 300 genes and biomarkers detected in your blood to identify potential treatment options for advanced cancer patients with solid tumors.

Genes
Segments of DNA. Genomic testing may find mutations in genes that can influence cancer growth.

Genomic Findings
Mutations identified in your cancer's DNA that may be matched with targeted treatment options.

Genomic Testing
You may also hear the testing referred to as biomarker testing, tumor testing, molecular testing, next-generation sequencing (NGS), and genomic profiling. Genomic testing is a general category of testing that looks for mutations in cancer genes to identify potential treatment options. Foundation Medicine performs a type of genomic testing called comprehensive genomic profiling (CGP).

Immunotherapy
A type of cancer treatment that helps the body's immune system attack cancer cells.

Liquid Biopsy
This type of testing is performed on a blood sample instead of a tissue sample. It looks at DNA from your tumor that is circulating in your blood.

Microsatellite Instability (MSI)
A biomarker that may help predict benefit from immunotherapy. MSI refers to a type of instability in a tumor's DNA.

Mutations
Changes in the DNA that can influence cancer growth (also called "alterations").

Targeted Therapy
A type of cancer treatment that attacks cancer cells with specific gene mutations.

Tumor
A mass within the body caused by abnormal growth of cells.

Tumor Fraction
An estimate of the percentage of DNA found in your blood sample that is tumor DNA.

Tumor Type
The type of cancer (e.g., lung cancer, breast cancer, etc.).

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. It is intended to help identify patients who may benefit from treatments with certain therapies. Use does not guarantee a match to treatment or that all relevant alterations will be found. Patients who are negative for companion diagnostic mutations should be reflexed to tumor tissue testing and mutation status confirmed using an FDA-approved tumor tissue test if feasible. For full use and risk information: www.foundationmedicine.com/patients.

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