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.
- A **GLOSSARY** of key terms is included on the last page of this guide.

Report Page One

1

Companion Diagnostic (CDx) Associated Findings

The FoundationOne Liquid CDx test for solid tumors is an FDA-approved "companion diagnostic" (or "CDx") for corresponding FDA-approved therapies (see definitions in glossary at end). This first layer of results (CDx-associated findings) is listed on page one. The "genomic findings detected" column includes the name of the gene where the mutation was found (e.g., "*PIK3CA*") along with a description of that mutation (e.g., "H1047L").

You and your doctor can discuss if any of the corresponding FDA-approved treatment options may be right for you.

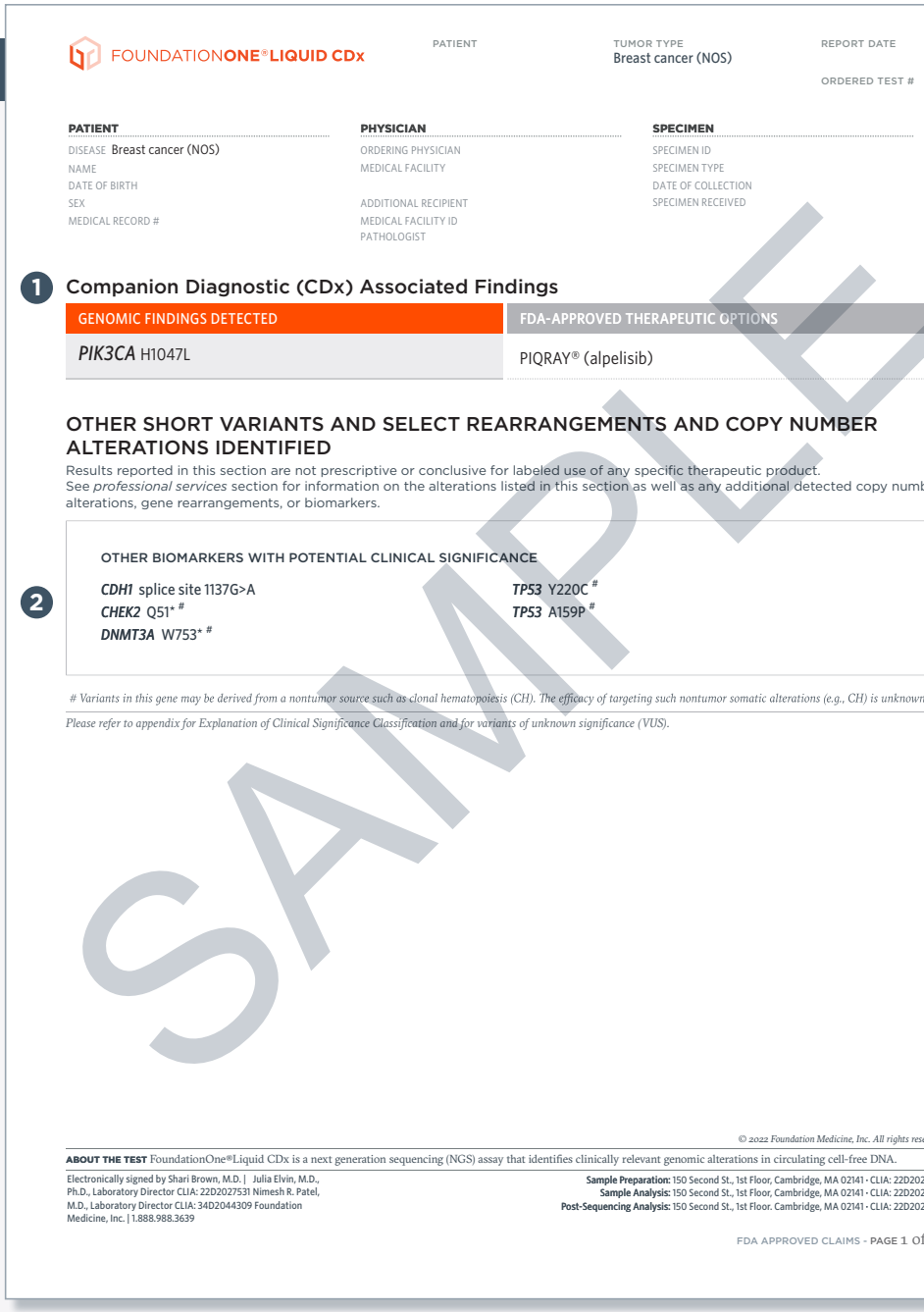
2

Other Biomarkers with Potential Clinical Significance

A second layer of results (beyond the CDx findings) are listed in this section. These findings, along with associated treatments, are described more on page two of the report.

What if there are no treatment options listed in the CDx section of my report?

This is not uncommon. If this applies for your report, you will see a gray box on this page stating "NO REPORTABLE ALTERATIONS WITH COMPANION DIAGNOSTIC (CDx) CLAIMS." There may be other treatment options on the following pages of your report, including FDA-approved therapies or clinical trials. Talk to your doctor about the treatment options in your full report.



FOUNDATIONONE®LIQUID CDx

PATIENT

TUMOR TYPE
Breast cancer (NOS)

REPORT DATE

ORDERED TEST #

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 **Companion Diagnostic (CDx) Associated Findings**

GENOMIC FINDINGS DETECTED	FDA-APPROVED THERAPEUTIC OPTIONS
PIK3CA H1047L	PIQRAY® (alpelisib)

OTHER SHORT VARIANTS AND SELECT REARRANGEMENTS AND COPY NUMBER ALTERATIONS IDENTIFIED

Results reported in this section are not prescriptive or conclusive for labeled use of any specific therapeutic product.
See *professional services* section for information on the alterations listed in this section as well as any additional detected copy numb
alterations, gene rearrangements, or biomarkers.

2 **OTHER BIOMARKERS WITH POTENTIAL CLINICAL SIGNIFICANCE**

CDH1 splice site 1137G>A
CHEK2 Q51* #
DNMT3A W753* #
TP53 Y220C #
TP53 A159P #

 # Variants in this gene may be derived from a nontumor source such as clonal hematopoiesis (CH). The efficacy of targeting such nontumor somatic alterations (e.g., CH) is unknown

Please refer to appendix for Explanation of Clinical Significance Classification and for variants of unknown significance (VUS).

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

Electronically signed by Shari Brown, M.D. | Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531 Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309 Foundation Medicine, Inc. | 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D202
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D202
Post-Sequencing Analysis: 150 Second St., 1st Floor. Cambridge, MA 02141 • CLIA: 22D202

Report Page Two

3

Biomarker Findings

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

4

Genomic Findings

This section shows the gene mutations that may be linked with treatment options, beyond the CDx findings on page one.

5

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.

6

Therapies with Clinical Relevance

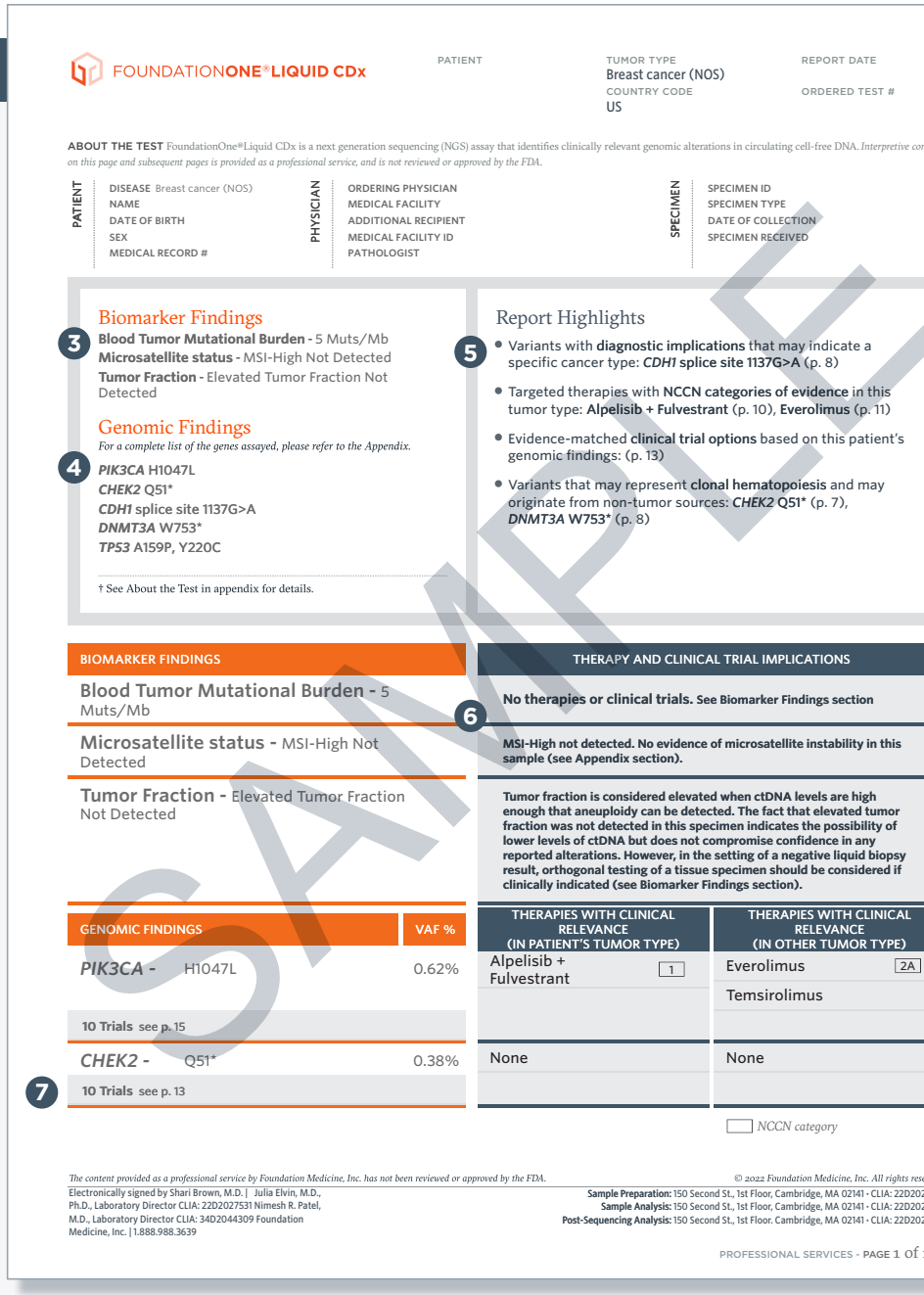
These are potential treatment options based on your genomic findings.

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.

7

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.



FOUNDATIONONE®LIQUID CDx

PATIENT

TUMOR TYPE
Breast cancer (NOS)
COUNTRY CODE
US

REPORT DATE

ORDERED TEST #

ABOUT THE TEST FoundationOne®Liquid CDx is a next generation sequencing (NGS) assay that identifies clinically relevant genomic alterations in circulating cell-free DNA. *Interpretive cor*
on this page and subsequent pages is provided as a professional service, and is not reviewed or approved by the FDA.

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

3 Biomarker Findings

Blood Tumor Mutational Burden - 5 Muts/Mb
Microsatellite status - MSI-High Not Detected
Tumor Fraction - Elevated Tumor Fraction Not Detected

4 Genomic Findings

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

PIK3CA H1047L
CHEK2 Q51*
CDH1 splice site 1137G>A
DNMT3A W753*
TP53 A159P, Y220C

† See About the Test in appendix for details.

5 Report Highlights

- Variants with **diagnostic implications** that may indicate a specific cancer type: ***CDH1* splice site 1137G>A** (p. 8)
- Targeted therapies with **NCCN categories of evidence** in this tumor type: **Alpelisib + Fulvestrant** (p. 10), **Everolimus** (p. 11)
- Evidence-matched **clinical trial options** based on this patient's genomic findings: (p. 13)
- Variants that may represent **clonal hematopoiesis** and may originate from non-tumor sources: ***CHEK2* Q51*** (p. 7), ***DNMT3A* W753*** (p. 8)

BIOMARKER FINDINGS
Blood Tumor Mutational Burden - 5 Muts/Mb
Microsatellite status - MSI-High Not Detected
Tumor Fraction - Elevated Tumor Fraction Not Detected

6 THERAPY AND CLINICAL TRIAL IMPLICATIONS

No therapies or clinical trials. See Biomarker Findings section

MSI-High not detected. No evidence of microsatellite instability in this sample (see Appendix section).

Tumor fraction is considered elevated when ctDNA levels are high enough that aneuploidy can be detected. The fact that elevated tumor fraction was not detected in this specimen indicates the possibility of lower levels of ctDNA but does not compromise confidence in any reported alterations. However, in the setting of a negative liquid biopsy result, orthogonal testing of a tissue specimen should be considered if clinically indicated (see Biomarker Findings section).

GENOMIC FINDINGS	VAF %	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
PIK3CA - H1047L	0.62%	Alpelisib + Fulvestrant [1]	Everolimus [2A]
			Temsirolimus
10 Trials see p. 15			
CHEK2 - Q51*	0.38%	None	None
7 **10 Trials** see p. 13			

NCCN category

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PROFESSIONAL SERVICES - PAGE 1 of

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.

The Rest of the Report

Your report contains additional pages with detailed information that your doctor can use to better understand your findings. This report guide is focused on the first two pages to help you understand the basics of your report. Remember, page one of your report describes the CDx associated findings and page two describes a second layer of options beyond the CDx findings. Read on to see a glossary of key terms discussed in this 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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