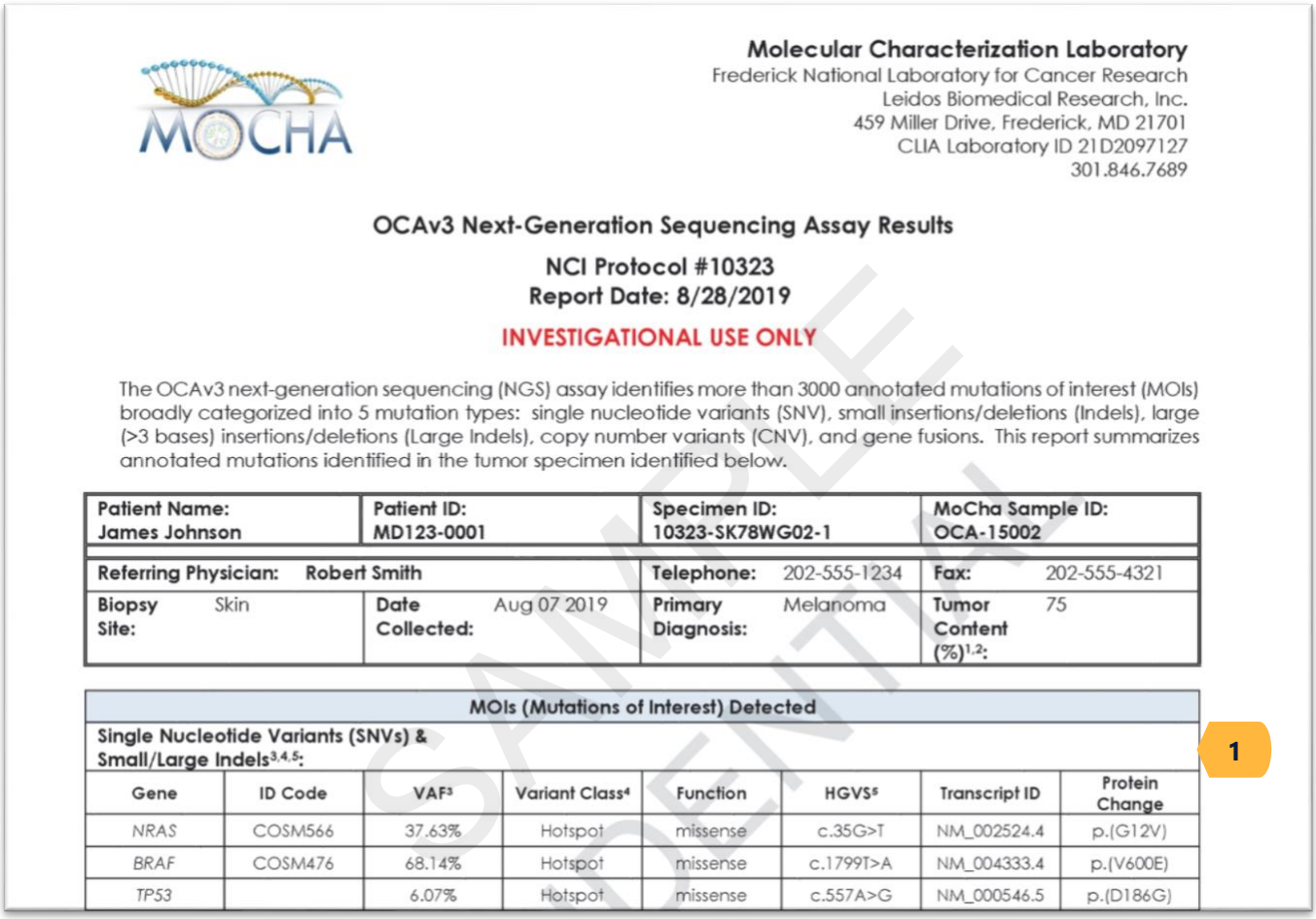
Guide to the MOCHA Solid Tumor Biomarker Report



MOCHA

Molecular Characterization Laboratory
Frederick National Laboratory for Cancer Research
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OCAv3 Next-Generation Sequencing Assay Results

NCI Protocol #10323
Report Date: 8/28/2019

INVESTIGATIONAL USE ONLY

The OCAv3 next-generation sequencing (NGS) assay identifies more than 3000 annotated mutations of interest (MOIs) broadly categorized into 5 mutation types: single nucleotide variants (SNV), small insertions/deletions (Indels), large (>3 bases) insertions/deletions (Large Indels), copy number variants (CNV), and gene fusions. This report summarizes annotated mutations identified in the tumor specimen identified below.

Patient Name: James Johnson	Patient ID: MD123-0001	Specimen ID: 10323-SK78WG02-1	MoCha Sample ID: OCA-15002
Referring Physician: Robert Smith		Telephone: 202-555-1234	Fax: 202-555-4321
Biopsy Site: Skin	Date Collected: Aug 07 2019	Primary Diagnosis: Melanoma	Tumor Content (%)[1,2]: 75

MOIs (Mutations of Interest) Detected

Single Nucleotide Variants (SNVs) & Small/Large Indels[3,4,5]:

Gene	ID Code	VAF[3]	Variant Class[4]	Function	HGVS[5]	Transcript ID	Protein Change
NRAS	COSM566	37.63%	Hotspot	missense	c.35G>T	NM_002524.4	p.(G12V)
BRAF	COSM476	68.14%	Hotspot	missense	c.1799T>A	NM_004333.4	p.(V600E)
TP53		6.07%	Hotspot	missense	c.557A>G	NM_000546.5	p.(D186G)

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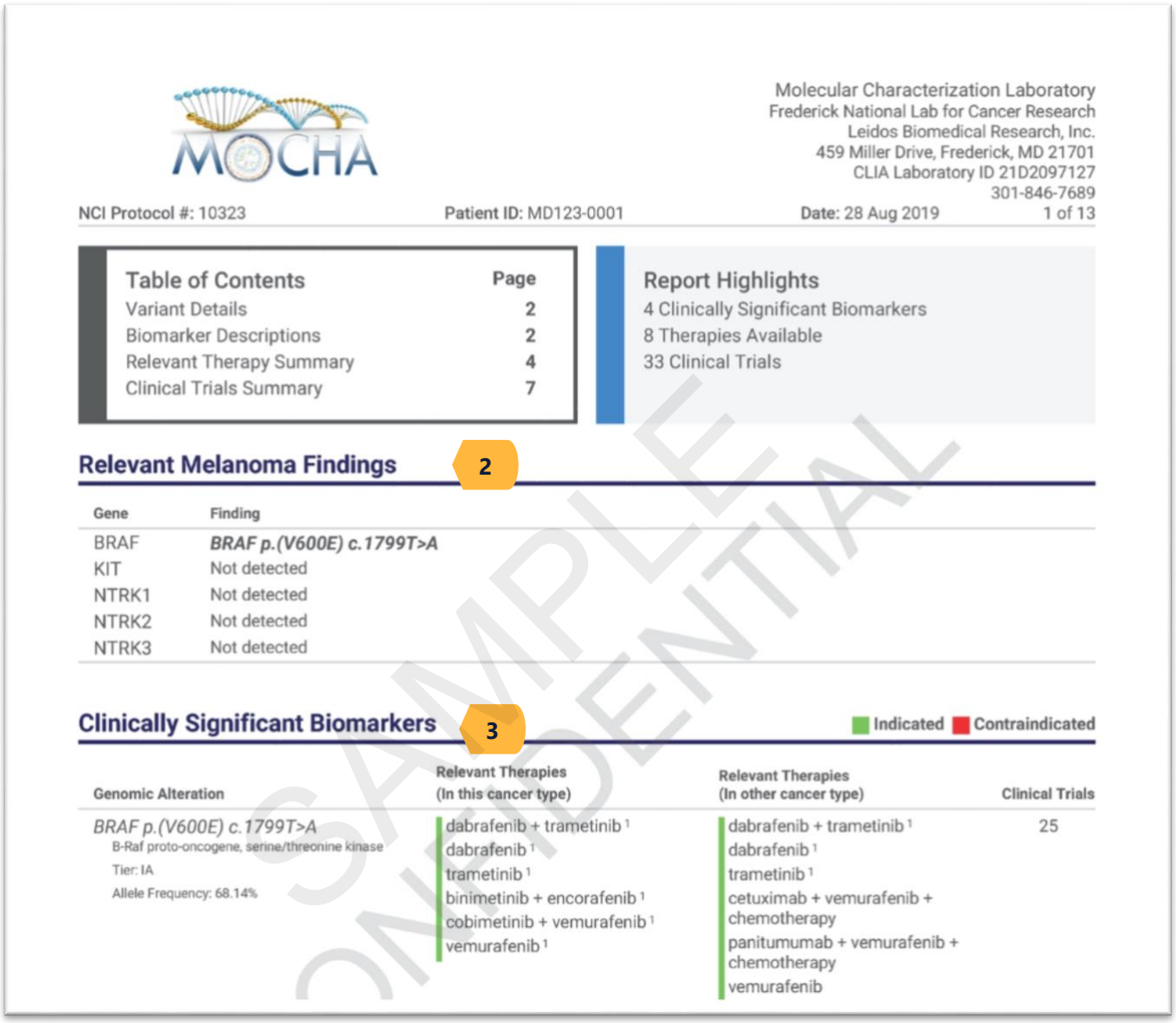
SAMPLE REPORT

1. Mutations of Interest (MOIs) Found in the Tumor

This table lists DNA and/or RNA biomarkers found in the tumor that may have important information about a person's cancer and possible treatments.

The biomarker test looks for three types of biomarkers:

- Single Nucleotide Variants – which are variations of a gene
- Copy Number Variants – which is the number of times a gene is repeated
- Gene fusions – when two separate genes combine together. Get more information on the genetics of cancer.



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Relevant Melanoma Findings 2

Gene	Finding
BRAF	*BRAF p.(V600E) c.1799T>A*
KIT	Not detected
NTRK1	Not detected
NTRK2	Not detected
NTRK3	Not detected

Clinically Significant Biomarkers 3 Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
BRAF p.(V600E) c.1799T>A B-Raf proto-oncogene, serine/threonine kinase Tier: IA Allele Frequency: 68.14%	dabrafenib + trametinib [1] dabrafenib [1] trametinib [1] binimetinib + encorafenib [1] cobimetinib + vemurafenib [1] vemurafenib [1]	dabrafenib + trametinib [1] dabrafenib [1] trametinib [1] cetuximab + vemurafenib + chemotherapy panitumumab + vemurafenib + chemotherapy vemurafenib	25

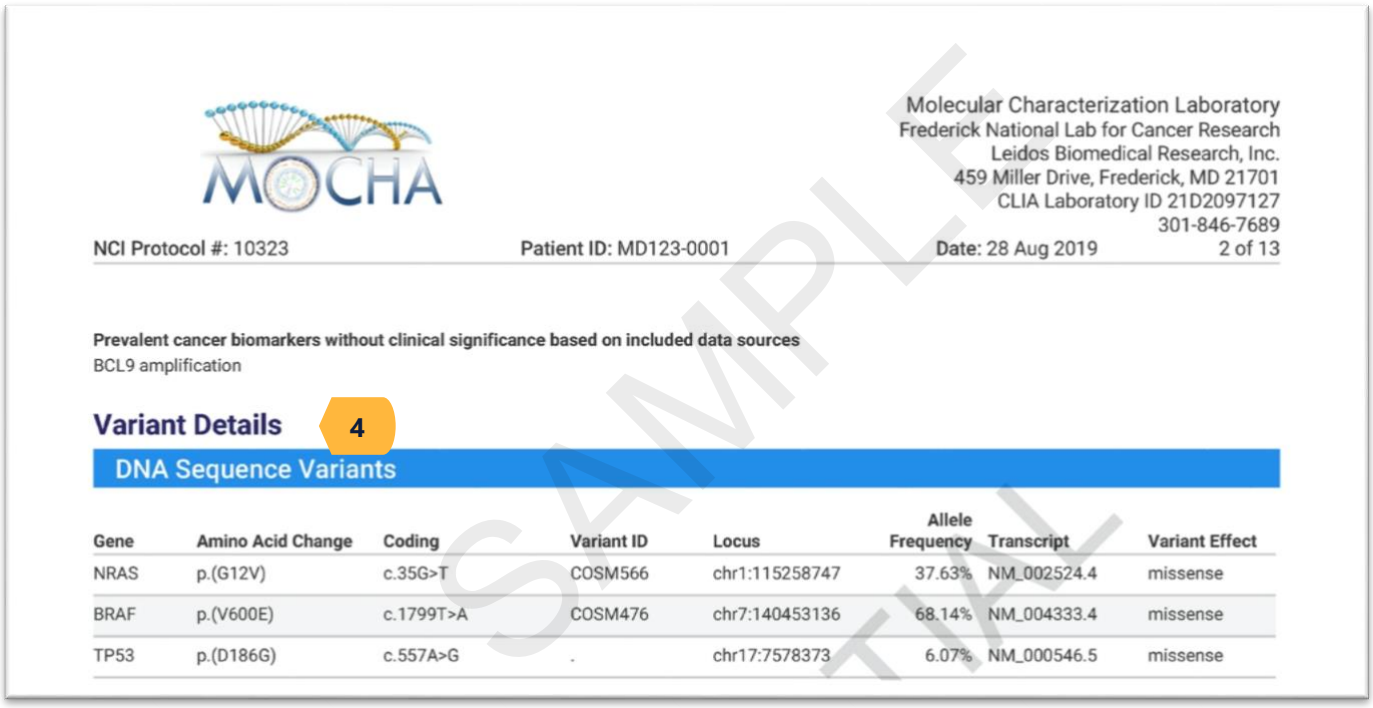
SAMPLE CONFIDENTIAL

2. Relevant Findings

This table lists key cancer genes tested for. If a gene tested for was found, the description and location of any gene mutations are included.

3. Clinically Significant Biomarkers

This table lists therapies (treatments) based on the cancer type and specific to biomarkers found in the tumor. The list includes therapies for the patient's specific cancer type as well as for other types of cancers that have the same biomarkers. Different cancer types that share biomarkers may respond to the same biomarker-targeted therapies.



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Prevalent cancer biomarkers without clinical significance based on included data sources
BCL9 amplification

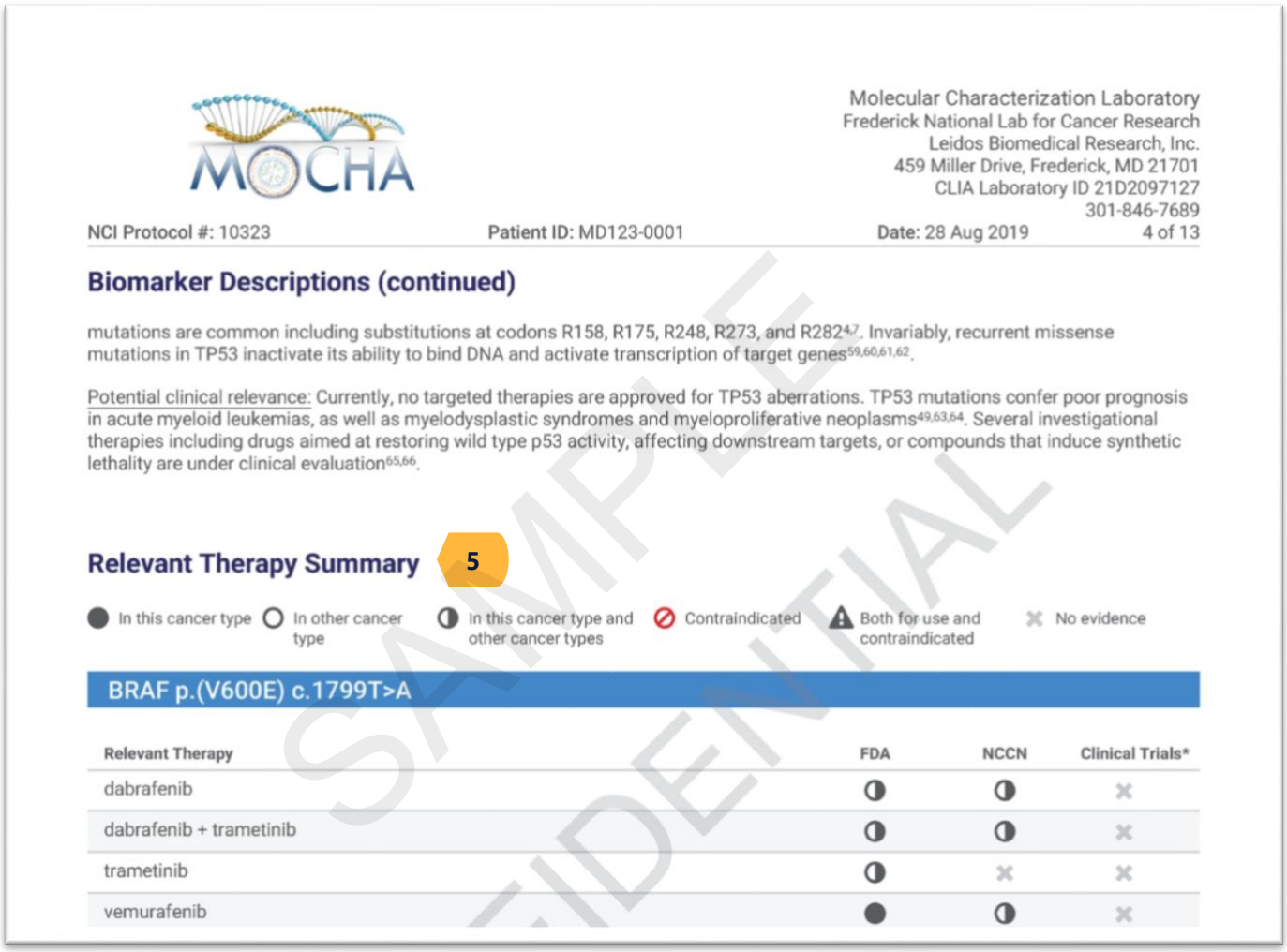
Variant Details 4

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
NRAS	p.(G12V)	c.35G>T	COSM566	chr1:115258747	37.63%	NM_002524.4	missense
BRAF	p.(V600E)	c.1799T>A	COSM476	chr7:140453136	68.14%	NM_004333.4	missense
TP53	p.(D186G)	c.557A>G	.	chr17:7578373	6.07%	NM_000546.5	missense

4. Variant Details

The biomarker report lists genes that are known to be related to cancer in some way. It also lists changes (variants) in those genes found in the tumor. Doctors may find this information useful when recommending treatment. There are still some changes in cancer genes that are not understood yet. They may be included in the report if they were detected, since they have been found in many cancers. This is another reason why research on these biomarkers is important.



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Biomarker Descriptions (continued)

mutations are common including substitutions at codons R158, R175, R248, R273, and R282[4,7]. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes[59,60,61,62].

Potential clinical relevance: Currently, no targeted therapies are approved for TP53 aberrations. TP53 mutations confer poor prognosis in acute myeloid leukemias, as well as myelodysplastic syndromes and myeloproliferative neoplasms[49,63,64]. Several investigational therapies including drugs aimed at restoring wild type p53 activity, affecting downstream targets, or compounds that induce synthetic lethality are under clinical evaluation[65,66].

Relevant Therapy Summary 5

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

BRAF p.(V600E) c.1799T>A

Relevant Therapy	FDA	NCCN	Clinical Trials*
dabrafenib	◑	◑	✖
dabrafenib + trametinib	◑	◑	✖
trametinib	◑	✖	✖
vemurafenib	●	◑	✖

5. Relevant Therapy Summary

The Food and Drug and Administration (FDA) and National Comprehensive Cancer Network (NCCN) publish therapy guidelines for specific cancer types. This table lists their recommended therapies based on the biomarkers found in the tumor. The table also shows whether there may be clinical trials available. A clinical trial is a type of research study that tests potential new therapies.

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Clinical Trials Summary 6

BRAF p.(V600E) c.1799T>A

NCT ID	Title	Phase
NCT02967692	A Randomized, Double-blind, Placebo-controlled, Phase III Study Comparing the Combination of PDR001, Dabrafenib and Trametinib Versus Placebo, Dabrafenib and Trametinib in Previously Untreated Patients With Unresectable or Metastatic BRAF V600 Mutant Melanoma	III
NCT02224781	DREAMseq (Doublet, Randomized Evaluation in Advanced Melanoma Sequencing) a Phase III Trial	III
NCT02231775	Neoadjuvant and Adjuvant Dabrafenib and Trametinib in Patients With Clinical Stage III Melanoma (Combi-Neo)	II
NCT03149029	A Phase II Trial of Abbreviated MAPK Targeted Therapy Plus Pembrolizumab in Patients With Unresectable or Metastatic Melanoma	II

6. Clinical Trials Summary

This table lists clinical trials that may be available for a specific type of cancer, based on gene mutations and or biomarkers found in the tumor. A clinical trial is a type of research study that tests potential new therapies.

More information on each clinical trial, such as where the clinical trial is being done, can be found at ClinicalTrials.gov.