MI PROFILE™
MOLECULAR INTELLIGENCE TUMOR REPORT

CARIS® LIFE SCIENCES

FINAL REPORT

PATIENT

Name: Patient, Test
Date of Birth: XX-Mon-19XX
Sex: Female
Case Number: TN17-XXXXXX
Diagnosis: Adenocarcinoma, NOS

SPECIMEN INFORMATION

Primary Tumor Site: Lung, NOS
Specimen Site: Lung, NOS
Specimen ID: ABC-1234-XX
Specimen Collected: XX-Mon-2017
Completion of Testing: XX-Mon-2017

ORDERED BY

Ordering Physician, MD
Cancer Center
123 Main Street
Springfield, XY 12345 USA
1 (123) 456-7890

BIOMARKER HIGHLIGHTS (SEE PAGE 2 AND APPENDIX FOR MORE DETAILS)

Biomarker	Method	Result
Lineage Relevant Biomarkers		
ALK	IHC	Negative | 0, 100%
	RNA-Seq	Fusion Not Detected
	NGS	Mutation Not Detected
ROS1	RNA-Seq	Fusion Not Detected
PD-L1	IHC	Positive, High Expression, TPS: 100%
EGFR	NGS	Mutation Not Detected
KRAS	NGS	Mutation Not Detected
BRAF	NGS	Mutation Not Detected
PIK3CA	NGS	Mutation Not Detected
Her2/Neu (ERBB2)	NGS	Mutation Not Detected

Biomarker	Method	Result
Lineage Relevant Biomarkers (cont)		
cMET	NGS	Mutated, Pathogenic
		Exon 14 | c.3082+1G>A
	RNA-Seq	Exon 14 Skipping Detected
	NGS	Amplification Not Detected
RET	RNA-Seq	Fusion Not Detected
Other Notable Biomarker Results		
Total Mutational Load		Low | 4 Mutations/Mb
MSI	NGS	Stable
BRCA2	NGS	Mutated, Pathogenic
		Exon 11 | V2228fs
TS	IHC	Positive | 1+, 20%
TUBB3	IHC	Positive | 2+, 95%

The therapies listed below are FDA-approved, on-NCCN Compendium® for the tested lineage or deemed relevant for this lineage by a panel of internal and external oncology experts. Complete therapy association information and Off-NCCN Compendium therapies are listed on pages (5-9).

THERAPIES WITH POTENTIAL BENEFIT

atezolizumab, nivolumab, pembrolizumab★‡‡	**PD-L1**
cabozantinib	cMET
carboplatin, cisplatin	BRCA2
crizotinib	cMET

See page 5 for off-NCCN compendium therapies.

★ Drug/biomarker association(s) supported by the highest level of clinical evidence.

‡‡ The PD-L1 result is sufficient to guide pembrolizumab use for front-line, metastatic & pretreated, metastatic NSCLC (nivolumab & atezolizumab are not FDA-approved in the front-line, metastatic setting).

THERAPIES WITH UNCERTAIN BENEFIT

docetaxel, nab-paclitaxel, paclitaxel	TUBB3
gemcitabine	RRM1
pemetrexed	TS

Drugs are placed in the Uncertain benefit category when a result suggests only a decreased likelihood of response (vs. little to no likelihood of response) or if there is insufficient evidence to associate the drug with either benefit or lack of benefit.

THERAPIES WITH POTENTIAL LACK OF BENEFIT

afatinib	EGFR, Her2/Neu (ERBB2)
alectinib, brigatinib, ceritinib	ALK
dabrafenib, trametinib, vemurafenib	BRAF
erlotinib, gefitinib	EGFR

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Therapies associated with potential benefit or lack of benefit are based on biomarker results and published medical evidence derived from multiple tumor types. The selection of any, all, or none of the matched therapies resides solely with the discretion of the treating physician. Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all available information concerning the patient's condition in accordance with the applicable standard of care.

CE

BIOMARKER RESULTS

This summary includes biomarkers most commonly associated with cancer. Complete details of all biomarkers tested can be found in the Appendix.

TOTAL MUTATIONAL LOAD

Mutations / Megabase: 4	Result: Low

MICROSATELLITE INSTABILITY (MSI) BY NEXT-GENERATION SEQUENCING

MSI by NGS	Result: Stable

GENES TESTED WITH MUTATIONS/ALTERATIONS

Gene	Method	Result	Alteration	Frequency (%)	Exon
BRCA2	NGS	Mutated, Pathogenic	V2228fs	46	11
cMET	NGS	Mutated, Pathogenic	c.3082+1G>A	14	14
	RNA-Seq	Exon 14 Skipping Detected	-	-	-

Unclassified alterations can be found in the Appendix

IMMUNOHISTOCHEMISTRY (IHC)

Biomarker	Result
ALK	Negative | 0, 100%
PD-L1	Positive, High Expression, TPS: 100%
PTEN	Positive | 1+, 100%

Biomarker	Result
RRM1	Positive | 2+, 55%
TOPO1	Positive | 2+, 100%
TS	Positive | 1+, 20%

Biomarker	Result
TUBB3	Positive | 2+, 95%

GENES TESTED WITH INDETERMINATE* SEQUENCING RESULTS BY NGS

PMS2	RAD50	SMARCE1									

* Genes in this table were ruled indeterminate due to low coverage for some or all exons. Please see Appendix for a complete list of indeterminate genes.

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Additional results continued on the next page. >

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GENES TESTED WITHOUT POINT MUTATIONS OR INDELS BY NGS

ABL1	AKT1	ALK	AMER1	APC	AR	ARAF	ARID1A	ARID2	ATM	ATRX	BAP1
BLM	BMPR1A	BRAF	BRCA1	BRIP1	c-KIT	CCND1	CDC73	CDH1	CDK4	CDKN1B	CDKN2A
CHEK1	CIC	CSF1R	CTNNB1	DDR2	DICER1	EGFR	ERBB3	ERBB4	ERCC2	ESR1	FANCC
FBXW7	FGFR1	FGFR2	FGFR3	FGFR4	FH	FLCN	FLT3	FOXL2	FUBP1	GATA3	GNA11
GNAQ	GNAS	Her2/Neu (ERBB2)	HIST1H3B	HNF1A	HRAS	IDH1	IDH2	JAK1	JAK2	JAK3	KDM5C
KDM6A	KDR (VEGFR2)	KMT2A	KMT2D	KRAS	MAX	MEK1	MEK2	MEN1	MITF	MLH1	MPL
MRE11A	MSH2	MSH6	MTOR	MUTYH	NBN	NF1	NF2	NPM1	NRAS	NTRK1	PALB2
PBRM1	PDGFRA	PDGFRB	PHOX2B	PIK3CA	PIK3R1	POLE	POT1	PPARG	PPP2R1A	PRKAR1A	PTCH1
PTEN	PTPN11	RAF1	RB1	RET	RNF43	ROS1	SDHAF2	SDHB	SDHC	SDHD	SETD2
SF3B1	SMAD2	SMAD4	SMARCA4	SMARCB1	SMO	SPOP	SRC	STK11	SUFU	TERT	TP53
TSC1	TSC2	VHL	WRN	WT1							

GENES TESTED WITHOUT COPY NUMBER VARIATIONS (AMPLIFICATIONS) BY NGS

AKT2	ALK	ARID1A	AURKB	CCND1	CCND3	CCNE1	CDK4	CDK6	CDK8	CDKN2A	cMET
CREBBP	CRKL	EGFR	EP300	EZH2	FGF10	FGF3	FGF4	FGFR1	FGFR2	FGFR3	GATA3
Her2/Neu (ERBB2)	KDR (VEGFR2)	MCL1	MDM2	MEK1	MYC	NF2	NFKBIA	NTRK1	RB1	RICTOR	ROS1
TOP1	WT1										

GENES TESTED WITH NO RNA ALTERATIONS BY NGS

Fusion Not Detected		Variant Transcript Not Detected
ALK	NTRK3	EGFRvIII
BRAF	RET	
NTRK1	ROS1	
NTRK2	RSPO3	

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NOTES OF SIGNIFICANCE

SEE APPENDIX FOR FULL DETAILS

A pathogenic frameshift mutation, V2228fs, was detected in BRCA2. This mutation (also known as c.6682dupG) has been reported as a germline mutation, causal for hereditary breast and ovarian cancer (ClinVar database). Correlation with patient's personal and familial cancer history is recommended. XX-Mon-2017

Clinical Trials Connector™ opportunities based on biomarker expression: 110 Chemotherapy Trials | 141 Targeted Therapy Trials. See page 10 for details.

Please note that the crizotinib association is based on a MET aberration and not based on ALK or ROS1 results.

SPECIMEN INFORMATION

Specimen ID: ABC-1234-XX

Specimen Collected: XX-Mon-2017

Specimen Received: XX-Mon-2017

Testing Initiated: XX-Mon-2017

Gross description: 1 (A) Paraffin Block - Client ID (ABC-123-XY) from XYZ Medical Center, Springfield, XY, with the corresponding cytology report labeled "ABC-123-XY".

Pathologic Diagnosis: Right lung nodule (core needle biopsy): Poorly differentiated non-small cell carcinoma, most consistent with adenocarcinoma.

Dissection Information: Molecular testing of this specimen was performed after harvesting of targeted tissues with an approved manual microdissection technique. Candidate slides were examined under a microscope and areas containing tumor cells (and separately normal cells, when necessary for testing) were circled. A laboratory technician harvested targeted tissues for extraction from the marked areas using a dissection microscope. The areas marked and extracted were microscopically reexamined on post-microdissected slides and adequacy of microdissection was verified by a board certified Pathologist.

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THERAPIES WITH **POTENTIAL BENEFIT**

Refer to the Appendix for detailed Result and Value information for each biomarker, including appropriate cutoffs, unit of measure, etc.

Therapies	Test	Method	Result	Value	Drug Association Details		
					Does Result Support Drug Association?	Highest Level of Evidence*	Reference
FDA-APPROVED/ON-NCCN COMPENDIUM®							
atezolizumab, nivolumab, pembrolizumab★	MSI	NGS	Stable	Stable	No	-	-
	PD-L1	IHC	Positive, High Expression ‡‡	TPS: 100%	Yes	I / Good	9#, 10#, 11, 12#, 13#
cabozantinib	cMET	NGS	Mutated, Pathogenic	c.3082+1G>A	Yes	II-3 / Good	14#
	cMET	RNA-Seq	Exon 14 Skipping Detected	-	Yes	II-3 / Good	14#
	RET	RNA-Seq	Fusion Not Detected	-	No	-	-
carboplatin, cisplatin	ATM	NGS	Mutation Not Detected	-	No	-	-
	BRCA1	NGS	Mutation Not Detected	-	No	-	-
	BRCA2	NGS	Mutated, Pathogenic	V2228fs	Yes	II-2 / Good	18, 19, 20

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Additional Therapies with Potential Benefit continued on the next page. >

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THERAPIES WITH **POTENTIAL BENEFIT**

Refer to the Appendix for detailed Result and Value information for each biomarker, including appropriate cutoffs, unit of measure, etc.

Therapies	Test	Method	Result	Value	Drug Association Details		
					Does Result Support Drug Association?	Highest Level of Evidence*	Reference
FDA-APPROVED/ON-NCCN COMPENDIUM®							
crizotinib	ALK	IHC	Negative	0+ 100%	No	-	-
	ALK	NGS	Mutation Not Detected	-	No	-	-
	ALK	RNA-Seq	Fusion Not Detected	-	No	-	-
	cMET	NGS	Amplification Not Detected	-	No	-	-
	cMET	NGS	Mutated, Pathogenic	c.3082+1G>A	Yes	II-3 / Good	14#, 21#
	cMET	RNA-Seq	Exon 14 Skipping Detected	-	Yes	II-3 / Good	14#, 21#
	ROS1	RNA-Seq	Fusion Not Detected	-	No	-	-
OFF-NCCN COMPENDIUM®							
irinotecan	TOPO1	IHC	Positive	2+ 100%	Yes	II-1 / Good	38, 39, 40
mitomycin-c	BRCA1	NGS	Mutation Not Detected	-	No	-	-
	BRCA2	NGS	Mutated, Pathogenic	V2228fs	Yes	II-3 / Good	41, 42, 43
olaparib	BRCA1	NGS	Mutation Not Detected	-	No	-	-
	BRCA2	NGS	Mutated, Pathogenic	V2228fs	Yes	I / Good	44, 45, 46, 47
oxaliplatin	ATM	NGS	Mutation Not Detected	-	No	-	-
	BRCA1	NGS	Mutation Not Detected	-	No	-	-
	BRCA2	NGS	Mutated, Pathogenic	V2228fs	Yes	II-2 / Good	18, 19, 20

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Additional Therapies with Potential Benefit continued on the next page. >

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TPS: Tumor Proportion Score; percentage of cells stained

★ Drug/biomarker association(s) supported by the highest level of clinical evidence.

‡‡ The PD-L1 result is sufficient to guide pembrolizumab use for front-line, metastatic & pretreated, metastatic NSCLC (nivolumab & atezolizumab are not FDA-approved in the front-line, metastatic setting).

* The level of evidence for all references is assigned according to the Literature Level of Evidence Framework consistent with the US Preventive Services Task Force described further in the Appendix of this report. The data level of each biomarker-drug interaction is the highest level of evidence based on the body of evidence, overall clinical utility, competing biomarker interactions and tumor type from which the evidence was gathered.

Evidence reference includes data from the same lineage as the tested specimen.

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THERAPIES WITH **UNCERTAIN BENEFIT**

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Therapies	Test	Method	Result	Value	Drug Association Details		
					Does Result Support Drug Association?	Highest Level of Evidence*	Reference
FDA-APPROVED/ON-NCCN COMPENDIUM®							
docetaxel, nab-paclitaxel, paclitaxel	TUBB3	IHC	Positive	2+ 95%	Yes	I / Good	29, 30#, 31#, 32#
gemcitabine	RRM1	IHC	Positive	2+ 55%	Yes	I / Good	37#
pemetrexed	TS	IHC	Positive	1+ 20%	Yes	II-1 / Good	15#, 16#, 17

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THERAPIES WITH **POTENTIAL LACK OF BENEFIT**

Refer to the Appendix for detailed Result and Value information for each biomarker, including appropriate cutoffs, unit of measure, etc.

Therapies	Test	Method	Result	Value	Drug Association Details		
					Does Result Support Drug Association?	Highest Level of Evidence*	Reference
FDA-APPROVED/ON-NCCN COMPENDIUM®							
afatinib	EGFR	NGS	Mutation Not Detected	-	Yes	I / Good	1#
	Her2/Neu (ERBB2)	NGS	Mutation Not Detected	-	Yes	I / Good	2#, 3#, 4#
alectinib, brigatinib, ceritinib	ALK	IHC	Negative	0+ 100%	Yes	II-1 / Good	5#, 6#, 7#, 8#
	ALK	RNA-Seq	Fusion Not Detected	-	Yes	II-1 / Good	5#, 6#, 7#, 8#
dabrafenib, trametinib, vemurafenib	BRAF	NGS	Mutation Not Detected	-	Yes	I / Good	22, 23, 24, 25#, 26#, 27, 28
erlotinib, gefitinib	cMET	NGS	Amplification Not Detected	-	No	-	-
	EGFR	NGS	Mutation Not Detected	-	Yes	I / Good	33#, 34#, 35#, 36#
	KRAS	NGS	Mutation Not Detected	-	No	-	-
	PIK3CA	NGS	Mutation Not Detected	-	No	-	-
	PTEN	IHC	Positive	1+ 100%	No	-	-

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Evidence reference includes data from the same lineage as the tested specimen.

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CLINICAL TRIALS CONNECTOR™

For a complete list of open, enrolling clinical trials visit MI Portal to access the **Clinical Trials Connector**. This personalized, real-time web-based service provides additional clinical trial information and enhanced searching capabilities, including, but not limited to:

- Location: filter by geographic area
- Biomarker(s): identify specific biomarkers associated with open clinical trials to choose from
- Drug(s): search for specific therapies
- Trial Sponsor: locate trials based on the organization supporting the trial(s)

Visit www.CarisMolecularIntelligence.com to view all matched trials.

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CHEMOTHERAPY CLINICAL TRIALS (110)

Drug Class	Biomarker	Method	Investigational Agent(s)
DNA minor groove binding agents (2)	BRCA2	NGS	PM01183 (lurbinectedin), trabectedin
Platinum compounds (92)	BRCA2	NGS	carboplatin, cisplatin
TOPO1 inhibitors (16)	TOPO1	IHC	irinotecan , topotecan

TARGETED THERAPY CLINICAL TRIALS (141)

Drug Class	Biomarker	Method	Investigational Agent(s)
cMET-targeted therapy (32)	cMET	NGS	AP26113, INC280, LY2801653, MGCD265, cabozantinib, crizotinib
Immunomodulatory agents (102)	PD-L1	IHC	MEDI4736, MK-3475, MPDL3280A, MSB0010718C, atezolizumab, avelumab, durvalumab, pembrolizumab
PARP inhibitors (7)	BRCA2	NGS	talazoparib, veliparib

( ) = represents the total number of clinical trials identified by the Clinical Trials Connector for the provided drug class or table.

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