OncoStrands™
Comprehensive Fusion Panel

PATIENT		PHYSICIAN	SPECIMEN	CASE
NAME John Doe	**SEX**	**ORDERING PHYSICIAN** Dr X	**EXT. SPECIMEN ID** **DATE RECEIVED** 25/01/2023	**ACCESSION#** RNAFusion_report_color_1
DATE OF BIRTH 25/01/2023	**MRN#** 12	**FACILITY** LifeStrands Genomics	**SPECIMEN TYPE** Blood specimen	**DATE REPORTED** **REVIEW STATUS** Final
DISEASE Non-small cell lung cancer		**DATE ORDERED** **COPY TO**	**% TUMOR CELLULARITY**	**REPORTED BY**
ADDRESS				

Report Summary

[Please add Executive Summary text here.]

IA	IB	IIC	IID	Trials
0	0	5	0	0

Clinical Implications

TIER	VARIANT DETECTED (GENE/SYNTAX)	CLINICAL IMPACT		SELECT CLINICAL TRIALS
IIC	HEY1, NCOA2 HEY1, NCOA2 fusion transcript	Diagnostic significance in:	Mesenchymal chondrosarcoma	0
IIC	HEY1, NCOA2 HEY1, NCOA2 fusion transcript	Diagnostic significance in:	Mesenchymal chondrosarcoma	0
IIC	HEY1, NCOA2 HEY1, NCOA2 fusion transcript	Diagnostic significance in:	Mesenchymal chondrosarcoma or Spindle cell rhabdomyosarcoma	0
IIC	HEY1, NCOA2 HEY1, NCOA2 fusion transcript	Diagnostic significance in:	Mesenchymal chondrosarcoma or Spindle cell rhabdomyosarcoma	0
IIC	HEY1, NCOA2 HEY1, NCOA2 fusion transcript	Diagnostic significance in:	Mesenchymal chondrosarcoma	0

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Other Test Results

[Please add Additional Comments here.]

Clinical Interpretations

HEY1, NCOA2	HEY1, NCOA2 fusion transcript	Tier IIC	VAF:	Depth:

HEY1 encodes a nuclear protein belonging to the hairy and enhancer of split-related (HESR) family of basic helix-loop-helix (bHLH) type transcriptional repressors and is an important downstream effector of Notch signaling (RefSeq, Jul 2008; UniProt.org). NCOA2 encodes a transcriptional coactivator for nuclear hormone receptors and acts as an intermediary factor for the ligand-dependent activity of these nuclear receptors (RefSeq, Mar 2016). The following associations with this genomic finding are from other tumor type contexts: An HEY1-NCOA2 fusion is of diagnostic value in mesenchymal chondrosarcoma per NCCN (Soft Tissue Sarcoma, 2.2022) guidelines. A HEY1-NCOA2 fusion is of diagnostic value in mesenchymal chondrosarcoma of bone per ESMO (PMID: 34500044, 2021) guidelines.

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type contexts: An HEY1–NCOA2 fusion is of diagnostic value in mesenchymal chondrosarcoma per NCCN (Soft Tissue Sarcoma, 2.2022) guidelines. A HEY1–NCOA2 fusion is of diagnostic value in mesenchymal chondrosarcoma of bone per ESMO (PMID: 34500044, 2021) guidelines.

Clinical Trials

No relevant clinical trials were reported.

Significant Negative Findings

[Please add your comments here.]

Tier III – Variants of Uncertain Significance

No variants were reported for this classification tier.

Other Comments

[Please add your comments here.]

Tier Definitions

Tier I-A: Approved therapy. Included in professional guidelines.
Tier I-B: Well-powered studies with consensus from experts in the field.
Tier II-C: Approved therapies for different tumour types or investigational therapies. Multiple small published studies with some consensus. Inclusion criteria for clinical trials.
Tier II-D: Limited clinical or preclinical studies.
Tier III (VUS): Variants of Unknown Clinical Significance.
Tier IV: Benign or likely benign variants (not included in the report)

Test Information

REPORTED GENES: A total of 501 genes were subjected to targeted next generation sequencing analysis. Details available upon request. **CGW VERSION:** CGW_v6.21.0.1 **DATABASE DETAILS:** The versions, releases, builds, dates of the following databases were used to generate this report: Genomic Build: GRCh37.p13 | Genomic Annotation Sources: NCBI RefSeq v105 | gnomAD: r2.1 | dbSNP: 149 | ExAC: v1.0 | NHLBI ESP: v.0.0.30 | COSMIC: v96 | dbNSFP: 4.3c | ClinVar: 20221001 | **ASSAY METHODOLOGY:**

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This assay, which is off the shelf Illumina TruSight™ RNA Fusion Panel, has been extensively validated in-house using commercial control material and clinical samples. The assay screens for known and novel fusion transcripts in 501 genes. The assay is validated for tumour tissue using formalin-fixed paraffin embedded (FFPE) tissue and cytology cell block.

A Pathologist reviews H&E-stained section of the tissue block or cell block to assess the adequacy of tumour cells and guides enrichment of tumour where needed for sequencing analysis. The in-house validation ensures that the sample passes all established laboratory QC metrics. Targeted next-generation sequencing is performed on RNA extracted by LifeStrands Genomics staff, followed by enrichment of RNA libraries and massively parallel sequencing performed on an Illumina NextSeq™ 550 instrument.

Secondary Analysis Method: The FASTQ files obtained from sequencing are analysed using the DRAGEN RNA app on Illumina BaseSpace Sequencing Hub. The obtained VCF files are then modified and uploaded using a customised analysis pipeline on to the Clinical Genomics WorkSpace (CGW) software platform from Pierian.

VARIANT CALLING: Variants are reported according to HGVS nomenclature (www.hgvs.org/mutnomen) and classified per the AMP classification system into tiers IA, IB, IIC, IID, III, and IV. These tiers are stratified by clinical utility ('actionability' for clinical decision-making as to diagnosis, prognosis, treatment options, and carrier status) and previously reported data in the medical literature. This assay only detects fusion aberrations and does not screen for copy number variations (CNVs) or mutations. Variants located outside of targeted regions will not be detected. It is possible that pathogenic variants may not be reported by one or more of the tools because of the parameters used. However, tool parameters were optimized to maximize specificity and sensitivity. The assay is not validated to detect copy number loss. The assay cannot differentiate between somatic and germline variants.

The OncoStrands™ Comprehensive Fusion Panel Gene List:

ABI1 ABL1 ABL2 ACACA ACE ACER1 ACKR3 ACSL6 ADD3 AFF1 AFF3 AFF4 AGR3 AHI1 AHRR ALK ANKRD28 AR ARHGAP2O ARHGAP26 ARNT ASPSCR1 ASTN2 ATF1 ATIC ATP1B4 AUTS2 BACH2 BAG4 BAIAP2L1 BAZ2A BCAS3 BCAS4 BCL1O BCL11A BCL11B BCL2 BCL2L1 BCL3 BCL6 BCL9 BCOR BCR BDNF BICC1 BIRC3 BIRC6 BRAF BRD1 BRD3 BRD4 BRWD3 BTBD18 BTG1 C11orf1 C11orf95 C2CD2L C3orf27 CAMTA1 CAPRIN1 CARS CASC5 CASP7 CBFA2T3 CBFB CBL CCAR2 CCDC28A CCDC6 CCDC88C CCNB1IP1 CCNB3 CCND1 CCND2 CCND3 CD74 CDH11 CDK5RAP2 CDK6 CDX1 CDX2 CEBPA CEBPB CEBPD CEBPE CEP17OB CEP85L CHD6 CHIC2 CHMP2B CHST11 CIC CIITA CLP1 CLTC CLTCL1 CMKLR1 CNBP CNOT2 CNTRL COG5 COL1A1 COL1A2 COL6A3 COX6C CPSF6 CRADD CREB1 CREB3L1 CREB3L2 CREBBP CRLF2 CRTC1 CSF1 CSF1R CTDSP2 CTNNB1 CUX1 DAB2IP DACH1 DACH2 DDIT3 DDX1O DDX2O DEK DMRT1 DNAJB1 DPM1 DUSP22 DUX4 EBF1 EEFSEC EGFR EGR1 EGR2 EGR3 EGR4 EIF4A2 ELF4 ELK4 ELL ELN EML1 EML4 EP3OO EP4OO EPC1 EPOR EPS15 ERBB3 ERC1 ERCC1 ERG ERLIN2 ESR1 ETS1 ETV1 ETV4 ETV5 ETV6 EWSR1 EZR FAM19A2 FCGR2B FCRL4 FEN1 FEV FGF8 FGFR1 FGFR1OP FGFR1OP2 FGFR2 FGFR3 FGFR4 FHIT FIP1L1 FLI1 FLNA FLT3 FLT3LG FNBP1 FOSB FOSL1 FOXO1 FOXO4 FOXP1 FRK FRYL FUS GAS7 GATA1 GIT2 GLI1 GOSR1 GOT1 GPR128 GPR34 GRHPR GRID1 GTF2I H2AFX HAS2 HEY1 HHEX HIP1 HIPK1 HIST1H4I HLF HMGA2 HNF1A HOXA1O HOXA11 HOXA13 HOXA9 HOXC11 HOXC13 HOXD11 HOXD13 HSP9OAA1 ID4 IKZF1 IL2 IL21R IL3 INPP5D IQCG IRF2BP2 IRF4 IRS4 ITK JAK1 JAK2 JAZF1 KANK1 KAT6A KAT6B KDM5A KIAA1524 KIF5B KMT2A KPNB1 KSR1 LASP1 LCK LCP1 LGR5 LHFP LHX2 LHX4 LMBRD1 LMO1 LMO2 LNP1 LPP LPXN LRMP LRRC37B LTBP1 LYL1 MACROD1 MAF MAFB MALT1 MAML2 MAPRE1 MBNL1 MBTD1 MDS2 MEAF6 MECOM MGEA5 MKL1 MKL2 MLF1 MLLT1 MLLT1O MLLT11 MLLT3 MLLT4 MLLT6 MN1 MNX1 MSI2 MSN MUC1 MUTYH MYB MYBL1 MYC MYH11 MYH9 MYO18A MYO1F NAB2 NAPA NBR1 NCOA1 NCOA2 NCOA3 NDE1 NF1 NFATC2 NFIB NGF NGFR NIN NIPBL NKX2-5 NONO NOTCH1 NPM1 NR4A3 NR6A1 NSD1 NT5C2 NTF3 NTF4 NTRK1 NTRK2 NTRK3 NUMA1 NUP1O7 NUP214 NUP98 NUTM1 NUTM2A NUTM2B OFD1 OLIG2 OLR1 OMD P2RY8 PAPPA PATZ1 PAX3 PAX5 PAX7 PAX8 PBX1 PCM1 PDE4DIP PDGFB PDGFRA PDGFRB PER1 PHF1 PHF23 PICALM PIM1 PLAG1 PML POM121 POU2AF1 POU5F1 PPAP2B PPARG PPARGC1A PPFIBP1 PPP2R1B PRCC PRDM16 PRKACA PRKAR1A PRKG2 PRRX2 PSIP1 PSMD2 PTPRR RABEP1 RAD51B RAF1 RANBP2 RAP1GDS1 RARA RBM15 RBM6 RCOR1 RCSD1 RET RHOH RNF213 ROS1 RPL22 RPN1 RREB1 RRM1 RTEL1 RUNX1 RUNX1T1 SARNP SEC31A 2-Sep 5-Sep 6-Sep 9-Sep SERPINE1 SERPINF1 SET SETBP1 SFPQ SH3D19 SH3GL1 SIK3 SLC34A2 SLC45A3 SLCO1B3 SMAP1 SMARCA5 SMARCB1 SORBS2 SORT1 SP3 SPECC1 SPTBN1 SQSTM1 SRF SRSF3 SS18 SS18L1 SSBP2 SSX1 SSX2 SSX4 ST6GAL1 STAT5B STAT6 STRN SUGP2 SUZ12 SYK TACC1 TACC2 TACC3 TAF15 TAL1 TAL2 TAOK1 TBX15 TCF12 TCF3 TCL1A TCTA TEAD1 TEAD2 TEAD3 TEAD4 TEC TENM1 TET1 TFE3 TFG TFPT TFRC TGFBR3 THADA THRAP3 TIRAP TLX1 TLX3 TMPRSS2 TNFRSF17 TOP1 TOP2B TP53BP1 TPM3 TPM4 TRHDE TRIM24 TRIP11 TRPS1 USP16 USP42 USP6 VGLL3 WASF2 WDR18 WDR7O WHSC1 WHSC1L1 WSB1 WT1 WWTR1 XIAP YAP1 YTHDF2 YWHAE ZBTB16 ZC3H7A ZC3H7B ZFP64 ZFPM2 ZFYVE19 ZMIZ1 ZMYM2 ZMYND11 ZNF2O7 ZNF384 ZNF444 ZNF521 ZNF585B ZNF687

DISCLAIMER: This is a laboratory developed test, and its performance characteristics have been determined by LifeStrands Genomics. NATA/RCPA accreditation does not currently cover the performance of this assay. This Report was generated using the materials and methods described above, which required the use of various reagents, protocols, instruments, software, databases, and other items, some of which were provided or made accessible by third parties. A defect or malfunction in any such reagents, protocols, instruments, software, databases, and or other items may compromise the quality or accuracy of the Report. The Report has been created based on, or incorporates references to, various scientific manuscripts, references, and other sources of information, including without limitation manuscripts, references, and other sources of information that were prepared by third parties that describe correlations between certain genetic mutations and particular diseases (and/or certain therapeutics that may be useful in ameliorating the effects of such diseases). Such information and correlations are subject to change over time in response to future scientific and medical findings. LifeStrands Genomics makes no representation or warranty of any kind, expressed or implied, regarding the accuracy of the information provided by or contained in such manuscripts, references, and other sources of information. If any of the information provided by or contained in such manuscripts, references, and other sources is later determined to be inaccurate, the accuracy and quality of the Report may be adversely impacted. LifeStrands Genomics is not obligated to

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