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TEST DESCRIPTIONS: (COMPREHENSIVE NGS AND OTHER BIOMARKERS ANALYSED BY TUMOR TYPE)

*Gene is also included in the RNA gene-fusion panel.

BLADDER CANCERS Bladder Multi-Omics™ **37 Genes** MSI and TMB


*ALK, AKT1, *AR, ATM, BAP1, *BRAF, BRCA1, BRCA2, CDKN2A, CCND1, CREBBP, *EGFR, ERBB2, ERBB3, ERBB4, FANCA, FBXW7, *FGFR1, *FGFR2, *FGFR3, HRAS, KDM6A, KMT2A, KMT2C, KMT2D, KRAS, MAP2K1, NF1, NRAS, PIK3CA, PTEN, RB1, *RET, SMARCA4, STAG2, TERT, TP53.

IHC Tests: MMR, PD-L1 (22C3).

BRAIN/CNS CANCERS Brain Multi-Omics™ **34 Genes** MSI and TMB


APC, ATRX, BRAF, CDK4, CTNNB1, CDKN2A, CDKN2B, EGFR, ERBB2, ERBB4, FGFR1, FGFR2, FGFR3, H3F3A, HRAS, IDH1, IDH2, NRG1, KIT, KRAS, MET, MTOR, MYCN, MYD88, NRAS, NTRK1, NTRK2, NTRK3, PDGFRA, TP53, TSC1, TSC2.

FISH Tests: 1p36/19q13, PTEN/CEN10. **IHC Tests:** MMR, PD-L1 (22C3).

BREAST CANCERS Breast Multi-Omics™ **43 Genes** TMB, MSI and HRD for PARPi efficacy


*AR, AKT1, ATM, *BRAF, BRCA1, BRCA2, CCNE1, CDH1, CDK12, CHEK1, CHEK2, *EGFR, ERBB2, ERBB3, ERBB4, *ESR1, FANCA, FANCL, *FGFR1, *FGFR2, *FGFR3, KRAS, MLH1, MRE11A, MSH2, MSH6, MUTYH, MYC, NBN, *NTRK1, *NTRK2, *NTRK3, PALB2, PIK3CA, PMS2, PTEN, RAD50, RAD51, RB1, *RET, STK11, TERT, TP53.

FISH Tests: HER-2/neu. **IHC Tests:** ER, HER-2/neu, Ki-67, MMR, PD-L1 (22C3), PR.

COLORECTAL CANCERS Colorectal Multi-Omics™ **38 Genes** MSI and TMB


AKT1, APC, ATM, AXIN2, *BRAF, CHEK1, CHEK2, ERBB2, ERBB3, ERBB4, *EGFR, FANCA, FBXW7, HRAS, KRAS, MAP2K1, *MET, MLH1, MSH2, MSH6, MUTYH, *NTRK1, *NTRK2, *NTRK3, NRAS, PIK3CA, PMS2, POLD1, POLE, PTEN, *RET, SMAD4, STK11, TERT, TP53.

FISH Tests: HER-2/neu. **IHC Tests:** BRAF, MMR, PD-L1 (22C3).

ENDOMETRIAL CANCERS Endometrial Multi-Omics™ **39 Genes** MSI and TMB


AKT1, APC, ARID1A, ARID2, ATM, *BRAF, BRCA1, BRCA2, CDK12, CDK4, CHEK2, CTNNB1, EPCAM, ERBB2, *ESR1, FBXW7, KRAS, MDM2, MLH1, MSH2, MSH6, NBN, NRAS, *NTRK1, *NTRK2, *NTRK3, PALB2, PIK3CA, PMS2, POLE, POLD1, PPP2R1A, PTEN, *RET, RNF43, SAMD4, STK11, TP53.

FISH Tests: HER-2/neu. **IHC Tests:** BRAF, MMR, PD-L1 (22C3).

ESOPHAGEAL CANCERS Esophagus Multi-Omics™ **34 Genes** MSI and TMB


AKT1, *AR, ARAF, ARID1A, *BRAF, CDK12, CDK6, CCNE1, CCND1, CDKN2A, *EGFR, ERBB2, ERBB3, *FGFR1, *FGFR2, *FGFR3, KIT, KRAS, MCL1, MAP2K1, *MET, MLH1, MSH2, MSH6, MTOR, *NTRK1, *NTRK2, *NTRK3, *NRG1, NRAS, PMS2, PIK3CA, *RET, TP53.

FISH Tests: HER-2/neu. **IHC Tests:** HER-2/neu, MMR, PD-L1 (22C3).

GASTRIC/GIST CANCERS Gastric/GIST Multi-Omics™ **40 Genes** MSI and TMB


*AR, APC, ATM, *BRAF, CD274, CDH1, CCNE1, CTNNB1, ERBB2, ERBB4, *EGFR, FBXW7, *FGFR1, *FGFR2, *FGFR3, KRAS, *MET, MDM2, MEN1, MLH1, MSH2, MSH6, NF1, *NRG1, NRAS, *NTRK1, *NTRK2, *NTRK3, PDGFRA, PIK3CA, PMS2, PTEN, *RET, RB1, SAMD4, SDHA, SDHB, SDHC, SDHD, TP53.

FISH Tests: HER-2/neu. **IHC Tests:** HER-2/neu, MMR, PD-L1 (22C3).

HEAD AND NECK CANCERS Head and Neck Multi-Omics™ **34 Genes** MSI and TMB


*AR, ATM, ARAF, *BRAF, CD274, CDKN2A, *EGFR, ERBB2, ERBB3, *FGFR1, *FGFR2, *FGFR3, HRAS, IDH1, IDH2, KRAS, *MET, MTOR, MLH1, MSH2, MSH6, NOTCH1, NRAS, *NRG1, *NTRK1, *NTRK2, *NTRK3, PIK3CA, PMS2, PTEN, *RSP02, *RET, TERT, TP53.

IHC Tests: MMR, PD-L1 (22C3).

HEPATOCELLULAR & BILIARY TRACT CANCERS Liver Multi-Omics™ **43 Genes** MSI and TMB


AKT1, ARAF, ARID1A, ATM, *BRAF, BAP1, BRCA1, BRCA2, CTNNB1, *EGFR, ERBB2, ERBB3, ERBB4, *ESR1, *FGFR1, *FGFR2, *FGFR3, FGFR4, GNAI1, IDH1, IDH2, KIT, KRAS, MAP2K1, MAP2K2, *MET, MLH1, MSH2, MSH6, MTOR, NRAS, *NRG1, *NTRK1, *NTRK2, *NTRK3, PALB2, PIK3CA, PMS2, PTEN, *RET, RAD51D, TERT, TP53.

IHC Tests: MMR, PD-L1 (22C3).

LUNG CANCERS Lung Multi-Omics™ **38 Genes** MSI and TMB


AKT1, *ALK, ARAF, ATM, *BRAF, ARID2, CCND1, CD274, CDK4, CDKN2A, CHEK2, ERBB2, ERBB3, *EGFR, *FGFR1, *FGFR2, *FGFR3, HRAS, KEAP1, KRAS, MAP2K1, *MET, MYCL, MTOR, NFE2L2, *NRG1, NRAS, *NTRK1, *NTRK2, *NTRK3, *NUTM1, PIK3CA, *RET, RICTOR, *ROSI, RB1, STK11, TP53.

FISH Tests: ALK, MET/CEN7, RET, ROS1. **IHC Tests:** ALK, BRAF, MMR, PD-L1 (22C3), ROS1.

MELANOMA Melanoma Multi-Omics™ **37 Genes** MSI and TMB


APC, ARID2, ATM, *BRAF, BAP1, BRCA2, CCND1, CDK4, CDKN2A, CHEK2, CTNNB1, EIF1AX, FBXW7, GNAI1, GNAQ, GNAS, IDH1, KIT, MAP2K1, MAP2K2, NF1, NRAS, *NTRK1, *NTRK2, *NTRK3, PALB2, PDGFRA, PIK3CA, PTEN, RB1, *RET, *ROSI, SF3B1, SMO, SRC, TERT, TP53.

IHC Tests: BRAF, MMR, PD-L1 (22C3).

OVARIAN CANCERS Ovarian Multi-Omics™ **43 Genes** TMB, MSI and HRD for PARPi efficacy


AKT1, ARAF, ATM, ARID1A, BARD1, *BRAF, BRCA1, BRCA2, BRIP1, CCNE1, CDK12, CHEK1, CHEK2, CTNNB1, ERBB2, *ESR1, FANCA, FANCL, *FGFR1, *FGFR2, *FGFR3, FOLR1, KIT, MAP2K1, *MET, MLH1, MSH2, MSH6, MTOR, *NTRK1, *NTRK2, *NTRK3, NF1, *NRG1, PALB2, PIK3CA, PMS2, PPP2R1A, PTEN, RAD51C, RAD51D, RAD54L, RET, TP53.

FISH Tests: HER-2/neu. **IHC Tests:** FOLR1, MMR, PD-L1 (22C3).

PANCREATIC CANCERS Pancreas Multi-Omics™ **29 Genes** TMB, MSI and HRD for PARPi efficacy


*ALK, ATM, *BRAF, BRCA1, BRCA2, CDKN2A, ERBB2, *FGFR1, *FGFR2, *FGFR3, FANCL, IDH1, IDH2, KRAS, MLH1, MSH2, MSH6, *NRG1, *NTRK1, *NTRK2, *NTRK3, PALB2, PMS2, PIK3CA, *RET, *ROSI, SMAD4, STK11, TP53.

IHC Tests: MMR, PD-L1 (22C3).

PROSTATE CANCERS Prostate Multi-Omics™ **42 Genes** TMB, MSI and HRD for PARPi efficacy


AKT1, *AR, ARID1A, ATM, ATR, BARD1, *BRAF, BRCA1, BRCA2, BRIP1, CCND1, CDK12, CHEK1, CHEK2, CTNNB1, FANCA, FANCD2, FANCL, HRAS, IDH1, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, *NTRK1, *NTRK2, *NTRK3, PALB2, PIK3CA, PMS2, PPP2R2A, PTEN, RAD51B, RAD51C, RAD51D, RB1, *RET, SPOP, TERT, TP53.

FISH Tests: PTEN/CEN10. **IHC Tests:** MMR, PD-L1 (22C3).

THYROID CANCERS Thyroid Multi-Omics™ **28 Genes** MSI and TMB


*ALK, AKT1, *BRAF, BRCA1, BRCA2, CDKN2A, CTNNB1, *FGFR1, *FGFR2, *FGFR3, HRAS, IDH1, IDH2, KRAS, MET, *NTRK1, *NTRK2, *NTRK3, NRAS, *RET, MLH1, MSH2, MSH6, PMS2, PALB2, PIK3CA, PTEN, TERT.

IHC Tests: BRAF, MMR, PD-L1 (22C3).

TUMOR OF UNKNOWN ORIGIN AND OTHERS Unknown Origin Multi-Omics™ **48 Genes** MSI and TMB


AKT1, ALK, AR, ARAF, BRAF, CD274, CDK4, CDKN2A, CHEK2, CTNNB1, EGFR, ERBB2, ERBB3, ERBB4, ERG, ESR1, ETV1, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, GNAI1, GNAQ, GNAS, HRAS, IDH1, IDH2, KIT, KRAS, MAP2K1, MAP2K2, MET, MTOR, NRAS, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PDGFRA, PIK3CA, PTEN, RAF1, RET, ROS1, SMO, TP53

IHC Tests: MMR, PD-L1 (22C3).

FOCUSED NGS PANEL

DNA hotspots					CNVs		RNA level gene fusions		Intra-genetic fusions
AKT1	CHEK2	FGFR3	KIT	NTRK3	ALK	FGFR3	ALK	NTRK2	AR-V7
AKT2	CTNNB1	FGFR4	KRAS	PDGFRA	AR	KRAS	BRAF	NTRK3	EGFR VIII
AKT3	EGFR	FLT3	MAP2K1	PIK3CA	CD274	MET	ESR1	NUTM1	MET exon 14 skipping
ALK	ERBB2	GNA11	MAP2K2	PTEN	CDKN2A	PIK3CA	FGFR1	RET	
AR	ERBB3	GNAQ	MET	RAF1	EGFR	PTEN	FGFR2	ROS1	
ARAF	ERBB4	GNAS	MTOR	RET	ERBB2		FGFR3	RSPO2	
BRAF	ESR1	HRAS	NRAS	ROS1	ERBB3		MET	RSPO3	
CDK4	FGFR1	IDH1	NTRK1	SMO	FGFR1		NRG1		
CDKN2A	FGFR2	IDH2	NTRK2	TP53	FGFR2		NTRK1		

DPYD PHARMACOGENOMICS INFORMED CONSENT

1. PURPOSE AND DESCRIPTION OF TESTING

- DPYD (dihydropyrimidine dehydrogenase) gene testing is a germline pharmacogenomic test that identifies inherited variants affecting your ability to metabolize fluoropyrimidine chemotherapy agents (5-fluorouracil [5-FU], capecitabine, tegafur).
- Results are used to guide safe dosing or selection of alternative therapy in accordance with CPIC (Clinical Pharmacogenomics Implementation Consortium) and FDA prescribing recommendations.
- This test analyzes clinically actionable DPYD variants including DPYD*2A (c.1905+1G>A, rs3918290), DPYD*13 (c.1679T>G, rs55886062), c.2846A>T (rs67376798), and DPYD HapB3 (c.1129-5923C>G, rs75017182). Additional DPYD variants may be analyzed depending on the assay performed. The variants assessed and testing methodology are specified in the laboratory report.
- Because DPYD variants are inherited (germline), results may have implications for biological relatives. Genetic counseling is available upon request.

2. POTENTIAL BENEFITS AND LIMITATIONS

- Benefits:** Identification of reduced-function variants may allow dose reduction or therapy modification to prevent severe or life-threatening fluoropyrimidine toxicity (e.g., mucositis, myelosuppression, neurotoxicity, hand-foot syndrome).
- Limitations:** A negative result does not eliminate all risk of fluoropyrimidine toxicity; other genetic and non-genetic factors may contribute. Current panels do not detect all known DPYD variants.
- Testing failure:** In rare cases, the assay may yield indeterminate results requiring repeat testing.

3. PRIVACY RIGHTS AND LEGAL PROTECTIONS

- GINA (Genetic Information Nondiscrimination Act, 2008, Pub.L. 110-233): Federal law prohibits health insurers and employers from discriminating based on genetic information. GINA does not apply to life insurance, disability insurance, or long-term care insurance.
- New Jersey Genetic Privacy Act (N.J.S.A. 10:5-43 et seq.): NJ law provides additional protections against genetic discrimination in insurance and employment. Disclosure of your genetic information requires your written authorization except as permitted by law.
- HIPAA: Your genetic test results are protected health information (PHI) and will be handled in accordance with applicable federal and state privacy regulations.
- Results will be reported to your ordering physician and incorporated into your medical record. Results will not be shared with third parties without your authorization except as required by law.

4. VOLUNTARY PARTICIPATION AND RIGHT TO DECLINE

- Participation in DPYD pharmacogenomic testing is voluntary. You may decline testing without penalty, though your physician may discuss how this affects your treatment plan.
- You have the right to withdraw consent at any time prior to sample processing. Once the sample has been analyzed, results cannot be recalled.
- If you choose not to undergo DPYD testing, standard fluoropyrimidine dosing per your physician's clinical judgment will apply.

5. SPECIMEN HANDLING AND STORAGE

- Testing will be performed on the peripheral blood specimen submitted with the accompanying siParadigm Solid Tumor Requisition Form.
- Residual specimen and/or extracted DNA may be retained for quality assurance purposes in compliance with CLIA/CAP retention requirements. Specimens will not be used for research without separate written consent.

PATIENT / LEGAL GUARDIAN CONSENT STATEMENT

I have read (or had read to me) the information above regarding DPYD pharmacogenomic testing. I have had the opportunity to ask questions and my questions have been answered to my satisfaction. I understand that this is a germline genetic test and that results may have implications for my biological relatives. I understand my rights under GINA and the New Jersey Genetic Privacy Act. I voluntarily consent to DPYD pharmacogenomic testing as ordered by my physician.

Patient / Legal Guardian Signature _____ *(MANDATORY FOR TESTING) Date _____

Relationship to Patient (if guardian) _____ Printed Name _____ Phone Number _____

ORDERING PHYSICIAN ATTESTATION

I have explained the nature, purpose, benefits, limitations, and privacy implications of DPYD pharmacogenomic testing to the patient or legal guardian. Informed consent has been obtained prior to specimen collection.

Ordering Physician Signature _____ *(MANDATORY FOR TESTING) Date _____

NPI Number _____ Printed Name _____ Specialty / Credentials _____

INSTRUCTIONS: This completed consent form must accompany the siParadigm Solid Tumor Requisition Form when DPYD pharmacogenomic testing is ordered. Results will be delayed if consent signature is missing. A copy should be retained in the patient's medical record.

Regulatory basis: New Jersey Genetic Privacy Act (N.J.S.A. 10:5-43); GINA (Pub.L. 110-233); CPIC DPYD Guideline (v1.4, 2023); FDA Table of Pharmacogenomic Biomarkers in Drug Labeling; CAP Molecular Pathology Checklist; CLIA 42 CFR §493.