

## Summit™ 2.0 Report

Patient Information	Provisional Diagnosis	Specimen	Physician Information
Name: Jane Doe DOB: 01/01/1990 Sex Assigned at Birth: Female MRN: 11xx22xx33	Diagnosis: Metastatic Breast Carcinoma; Central Nervous System Neoplasm ICD10: C79.31	Type: CSF Collected: 01/01/2026 Received: 01/02/2026 Specimen ID: SumOnlyPos-Mets	Institution: Belay Diagnostics Referring Physician: Provider Test

### RESULT SUMMARY

## POSITIVE

Comments
<p><i>ERBB2</i> (HER2) amplification is a predictive diagnostic and therapeutic marker for central nervous system metastases from breast carcinoma (WHO, see Actionability Summary). <i>TP53</i> is the most commonly mutated gene in breast cancer with alterations observed at higher frequencies in breast cancer brain metastasis and aggressive disease (PMID: 26527317, 26527317, 22187033). <i>ARID1A</i> variants are reported in approximately 4-7% of breast cancer cases and may be associated with resistance to endocrine therapy (PMID: 41514650, 31932695, 34804958). Clinical correlation is required.</p> <p>NOTE: Summit™ 2.0 does NOT include evaluation of chromosomal arm-level and focal gains/losses. Aneuploidy analysis can be performed for this specimen with clinician authorized order of Ascent™. Please contact customer service (phone: 331-320-0155, email: customer.service@belaydiagnostics.com) to order the test; no additional sample is needed.</p>

### CLINICALLY SIGNIFICANT ALTERATION DETAILS (Tier 1 or 2 per AMP/ASCO/CAP)

SNV, MNV, Indel Variants				
Alteration	VAF	Actionability Summary		
		FDA/NCCN Therapies Associated	Prognostic/Diagnostic Guidelines	Clinical Trial Options
<i>ARID1A</i> p.Q185* c.553C>T	0.6%	No	No	Yes
<i>TP53</i> p.R342* c.1024C>T	45.4%	No	Yes	Yes

Copy Number Variants					
Alteration	Location	Fold Change	Actionability Summary		
			FDA/NCCN Therapies Associated	Prognostic/Diagnostic Guidelines	Clinical Trial Options
<i>ERBB2</i> Amplification	chr17	5.66	Yes	No	Yes

**Fusion Variants:** None

Biomarkers					
Tumor Mutation Burden (TMB)			Microsatellite Instability (MSI)		
Not Detected	Low	High	Stable	High	

### VARIANTS OF UNKNOWN SIGNIFICANCE (Tier 3)

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SNV/MNVs/Indels			
AURKB M298T CHD4 R1732W FANCA E38Q	FANCC R245Q GLI1 A670S JAK1 E186Q	MAP3K4 G742E PAK5 R352M PRDM1 S654F	PRKDC R36H RICTOR R907L

Gene Level CNVs
None

Fusions
None

### ACTIONABILITY SUMMARY

FDA / NCCN Therapies for the Patient's Tumor Type (Tier 1A)			
Biomarker	Therapies	Setting	Source(s)
ERBB2 Amplification	pertuzumab + trastuzumab +/- (paclitaxel or docetaxel)	First line	FDA (Approved), NCCN
ERBB2 Amplification	ado-trastuzumab emtansine; pertuzumab/trastuzumab/hyaluronidase; trastuzumab +/- chemotherapy; trastuzumab/hyaluronidase	Metastatic	FDA (Approved), NCCN
ERBB2 Amplification	fam-trastuzumab deruxtecan	Unresectable or metastatic	FDA (Approved), NCCN
ERBB2 Amplification	fam-trastuzumab deruxtecan	Subsequent line, and no satisfactory alternative therapy	FDA (Approved)
ERBB2 Amplification	lapatinib + capecitabine; margetuximab + chemotherapy; neratinib + capecitabine; trastuzumab + tucatinib + capecitabine	Subsequent line	FDA (Approved), NCCN
ERBB2 Amplification	lapatinib + trastuzumab	Metastatic	NCCN

FDA / NCCN Therapies with Resistance / Decreased Response (Tier 1A): None
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Prognostic Implications per NCCN: None
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Diagnostic Implications per WHO		
Biomarker	Diseases	Note
TP53 R342*	Breast Neoplasm	TP53 mutations are common in breast cancer, though they occur with varying frequencies in different subtypes. In particular, TP53 mutations are most frequent in the ER-negative pathway (PMID: 23000897), including both HER2-positive and HER2-negative groups. In triple-negative breast cancer, basal-like tumors have frequent TP53 mutations (84%), with the basal-like 1 subtype showing a very high rate (92%). TP53 mutations are notably less frequent in lobular carcinoma in situ, malignant adenomyoepithelioma (AME-M), and adenoid cystic carcinoma.


### CLINICAL TRIALS / INVESTIGATIONAL THERAPIES

ARID1A Q185*			
Therapy	Clinical Trial	Location/Sponsor	WeTrials


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JAB-2485	<a href="#">NCT05490472</a> (Phase 1/Phase 2) JAB-2485 Activity in Adult Patients With Advanced Solid Tumors	Detroit, Michigan Jacobio Pharmaceuticals Co., Ltd. <a href="mailto:clinicaltrials@jacobiopharma.com">clinicaltrials@jacobiopharma.com</a>	  <a href="https://genomonology.wetrial.com/v1/NCT05490472">https://genomonology.wetrial.com/v1/NCT05490472</a>
talazoparib	<a href="#">NCT04550494</a> (Phase 2) Measuring the Effects of Talazoparib in Patients With Advanced Cancer and DNA Repair Variations	Gainesville, Florida National Cancer Institute (NCI)	  <a href="https://genomonology.wetrial.com/v1/NCT04550494">https://genomonology.wetrial.com/v1/NCT04550494</a>
tazemetostat	<a href="#">NCT05023655</a> (Phase 2) Phase II Study of Tazemetostat in Solid Tumors Harboring an ARID1A Mutation	Greenville, South Carolina Prisma Health-Upstate <a href="mailto:julie.martin@prismahealth.org">julie.martin@prismahealth.org</a>	  <a href="https://genomonology.wetrial.com/v1/NCT05023655">https://genomonology.wetrial.com/v1/NCT05023655</a>
tulmimetostat	<a href="#">NCT04104776</a> (Phase 1/Phase 2) A Study of Tulmimetostat DZR123 (CPI-0209) in Patients With Advanced Solid Tumors and Lymphomas	Atlanta, Georgia Novartis Pharmaceuticals <a href="mailto:novartis.email@novartis.com">novartis.email@novartis.com</a>	  <a href="https://genomonology.wetrial.com/v1/NCT04104776">https://genomonology.wetrial.com/v1/NCT04104776</a>





### ARID1A Q185\* + TP53 R342\*



Therapy	Clinical Trial	Location/Sponsor	WeTrials
LP-184	<a href="#">NCT05933265</a> (Phase 1/Phase 2) Study of LP-184 in Patients with Advanced Solid Tumors	Springdale, Arkansas Lantern Pharma Inc. <a href="mailto:lyza@lanternpharma.com">lyza@lanternpharma.com</a>	  <a href="https://genomonology.wetrial.com/v1/NCT05933265">https://genomonology.wetrial.com/v1/NCT05933265</a>

### ERBB2 Amplification

Therapy	Clinical Trial	Location/Sponsor	WeTrials
GLSI-100	<a href="#">NCT05232916</a> (Phase 3) Phase 3 Study to Evaluate the Efficacy and Safety of HER2/Neu Peptide GLSI-100 (GP2 + GM-CSF) in HER2/Neu Positive Subjects	Tucson, Arizona Greenwich LifeSciences, Inc. <a href="mailto:Jaye.Thompson@GreenwichLifeSciences.com">Jaye.Thompson@GreenwichLifeSciences.com</a>	  <a href="https://genomonology.wetrial.com/v1/NCT05232916">https://genomonology.wetrial.com/v1/NCT05232916</a>

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carvedilol	<b>NCT03418961</b> (Phase 3) S1501 Dual Observational and Randomized Cohort Study of Patients With Metastatic HER-2+ Breast Cancer at Risk of Cardiac Toxicity	Duarte, California SWOG Cancer Research Network	 <a href="https://genomoncology.wetrials.com/v1/NCT03418961">https://genomoncology.wetrials.com/v1/NCT03418961</a>
trastuzumab + liposomal doxorubicin + paclitaxel	<b>NCT00294996</b> (Phase 3) Trial of Myocet in Metastatic Breast Cancer	San Diego, California Sopherion Therapeutics	 <a href="https://genomoncology.wetrials.com/v1/NCT00294996">https://genomoncology.wetrials.com/v1/NCT00294996</a>
zanidatamab + (capecitabine or eribulin or gemcitabine or vinorelbine)	<b>NCT06435429</b> (Phase 3) A Study Comparing the Efficacy and Safety of Zanidatamab to Trastuzumab, Each in Combination With Physician's Choice Chemotherapy, for the Treatment of Participants With Metastatic HER2-positive Breast Cancer	Phoenix, Arizona Jazz Pharmaceuticals <a href="mailto:ClinicalTrialDisclosure@JazzPharma.com">ClinicalTrialDisclosure@JazzPharma.com</a>	 <a href="https://genomoncology.wetrials.com/v1/NCT06435429">https://genomoncology.wetrials.com/v1/NCT06435429</a>
zongertinib	<b>NCT06581432</b> (Phase 2) Beamion PANTUMOR-1: A Study to Test Whether Zongertinib Helps People With Advanced Cancers With HER2 Alterations	Anchorage, Alaska Boehringer Ingelheim <a href="mailto:clintriage.rdg@boehringer-ingelheim.com">clintriage.rdg@boehringer-ingelheim.com</a>	 <a href="https://genomoncology.wetrials.com/v1/NCT06581432">https://genomoncology.wetrials.com/v1/NCT06581432</a>

TP53 R342*			
Therapy	Clinical Trial	Location/Sponsor	WeTrials
AO-252	<b>NCT06136884</b> (Phase 1) A First-In-Human, Phase 1 Study Evaluating Oral TACC3 PPI Inhibitor, AO-252, in Advanced Solid Tumors With or Without Brain Metastases	Detroit, Michigan A2A Pharmaceuticals Inc. <a href="mailto:rfrnka@coiledtx.com">rfrnka@coiledtx.com</a> ; <a href="mailto:rfrnka@a2apharma.net">rfrnka@a2apharma.net</a>	 <a href="https://genomoncology.wetrials.com/v1/NCT06136884">https://genomoncology.wetrials.com/v1/NCT06136884</a>
anti-KRAS and anti-TP53 peripheral blood lymphocytes + aldesleukin + cyclophosphamide + fludarabine; anti-KRAS and anti-TP53 peripheral blood lymphocytes + pembrolizumab + aldesleukin + cyclophosphamide + fludarabine	<b>NCT03412877</b> (Phase 2) Administration of Autologous T-Cells Genetically Engineered to Express T-Cell Receptors Reactive Against Neoantigens in People With Metastatic Cancer	Bethesda, Maryland National Cancer Institute (NCI) <a href="mailto:IRC@nih.gov">IRC@nih.gov</a>	 <a href="https://genomoncology.wetrials.com/v1/NCT03412877">https://genomoncology.wetrials.com/v1/NCT03412877</a>

### TIER 1A THERAPY DETAILS

ERBB2 Amplification		
Therapy	Approval / Guideline Summary	Underlying Evidence

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ado-trastuzumab emtansine	FDA approved for HER2-positive, metastatic breast cancer that previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy. NCCN recommended as Category 2A.	In a Phase III trial (EMILIA) that supported FDA approval, treatment with Kadcyca (trastuzumab emtansine) improved median progression free survival (9.6 mo vs 6.4 mo) and overall survival (30.9 mo vs 25.1 mo) compared to Tykerb (lapatinib) combined with Xeloda (capecitabine) in patients with metastatic ERBB2 (HER2)-positive breast cancer (PMID: 24879797, PMID: 23020162; NCT00829166). In a Phase II (MATCH) trial, Kadcyca (trastuzumab emtansine) treatment resulted in partial response in 8.1% (3/37) and stable disease in 43% (16/37) of patients with ERBB2 (HER2) amplified non-breast, non-gastric advanced solid tumors, with a 6-month progression-free survival rate of 24.8% (J Clin Oncol 36, 2018 (suppl; abstr 100); NCT02465060).
fam-trastuzumab deruxtecan	FDA approved for adults with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either in the metastatic setting, or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within 6 months of completing therapy. NCCN recommended for subsequent line or first line therapy (Category 1/Preferred intervention).	The FDA approval for fam-trastuzumab deruxtecan was supported by data from the open-label, randomized, phase-III trial DESTINY-Breast03 (NCT03529110). DESTINY-Breast03 demonstrated that subsequent-line fam-trastuzumab deruxtecan, compared with ado-trastuzumab emtansine, improved median PFS (HR = 0.28, p < 0.0001; NR (n = 261) vs. 6.8 mo. (n = 263)) in patients with metastatic or unresectable, HER2+ breast carcinoma. The secondary endpoint was ORR (82.7% vs. 36.1%). The FDA approval for fam-trastuzumab deruxtecan was also supported by data from the single-arm, phase-II trial DESTINY-Breast01 (NCT03248492; PMID: 31825192). DESTINY-Breast01 demonstrated that subsequent-line fam-trastuzumab deruxtecan had an ORR of 60.3% (n = 184; CR, 4.3%; PR, 56.0%) and a median DoR of 14.8 mo. (n = 184) in patients with metastatic or unresectable, HER2+ breast carcinoma.
fam-trastuzumab deruxtecan	FDA approved for unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options.	The FDA approval for fam-trastuzumab deruxtecan was supported by data from three clinical trials: DESTINY-PanTumor02 (NCT04482309), DESTINY-Lung01 (NCT03505710), and DESTINY-CRC02 (NCT04744831). Data from the open-label, multi-cohort, phase-II trial DESTINY-PanTumor02 demonstrated that subsequent-line fam-trastuzumab deruxtecan (n = 111) conferred an ORR of 51.4% (CR = 2.7%, PR = 48.6%) and a median DoR of 19.4 mos. in patients with unresectable or metastatic HER2-positive solid tumors. Data from the open-label, two-cohort, phase-II trial DESTINY-Lung01 demonstrated that subsequent-line fam-trastuzumab deruxtecan (n = 17) conferred an ORR of 52.9% (CR = 5.9%, PR = 47.1%) and a median DoR of 6.9 mos. in patients with relapsed/refractory, unresectable, or metastatic HER2-positive NSCLC. Data from the randomized, two-arm, phase-II trial DESTINY-CRC02 demonstrated that subsequent-line fam-trastuzumab deruxtecan (n = 64) conferred an ORR of 46.9% (CR = 0%, PR = 46.9%) and a median DoR of 5.5 mos. in patients with relapsed/refractory, unresectable, or metastatic HER2-positive CRC.
lapatinib + capecitabine	FDA approved for advanced or metastatic breast cancer that overexpresses HER2 and that had prior therapy including an anthracycline, a taxane, and trastuzumab. NCCN recommended as Category 2A.	The FDA approval for lapatinib + capecitabine was supported by data from the randomized, phase-III trial NCT00078572 (PMID: 17192538). NCT00078572 demonstrated that subsequent-line lapatinib + capecitabine, compared with capecitabine, improved median time to progression (HR = 0.57; p = 0.00013; 27.1 weeks vs. 18.6 weeks) in patients with locally advanced or metastatic, HER2-Positive BCa. The secondary endpoint was median OS (75.0 weeks vs. 65.9 weeks).
lapatinib + trastuzumab	NCCN recommended as subsequent line therapy for unresectable, recurrent, or metastatic HER2-positive breast cancer, without cytotoxic therapy (Category 2A).	
margetuximab + chemotherapy	FDA approved for metastatic HER2-positive breast cancer that received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease. NCCN recommended as Category 2A.	In a Phase III trial (SOPHIA) that supported FDA approval, Margenza (margetuximab-cmkb) in combination with chemotherapy resulted in improved primary progression-free survival (5.8 vs 4.9 mo, HR=0.76, p=0.03) compared to Herceptin (trastuzumab) plus chemotherapy in patients with ERBB2 (HER2)-positive (IHC 3+ or FISH amplified) metastatic breast cancer whose disease progressed after two or more lines of anti-ERBB2 (HER2) therapies (PMID: 33480963; NCT02492711).
neratinib + capecitabine	FDA approved for advanced or metastatic HER2-positive breast cancer that had two or more prior anti-HER2 based regimens in the metastatic setting. NCCN recommended as Category 2A.	In a Phase III (NALA) trial that supported FDA approval, combination of Nerlynx (neratinib) and Xeloda (capecitabine) reduced risk of disease progression or death (HR=0.76, p=0.006), improved 12-month PFS (28.8%, 88 /307 vs 14.8%, 46/314) compared to lapatinib and capecitabine combination in patients with metastatic ERBB2 (HER2)-positive (amp/over exp) breast cancer who had 2 or more prior ERBB2 (HER2)-targeted therapies (J Clin Oncol 37, no. 15_suppl (May 20, 2019) 1002-1002; NCT01808573).

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pertuzumab + trastuzumab +/- (paclitaxel or docetaxel)	FDA approved with paclitaxel for HER2-positive metastatic breast cancer that has not received prior anti-HER2 therapy or chemotherapy for metastatic disease. NCCN recommended as a Preferred intervention (Category 1 for docetaxel, Category 2A for paclitaxel). Per NCCN, may also be considered if previously treated with trastuzumab plus chemotherapy in the absence of pertuzumab.	The FDA approval for pertuzumab + trastuzumab +/- (docetaxel or paclitaxel) was supported by data from the double-blind, placebo-controlled, phase-III trial CLEOPATRA (NCT00567190; PMID: 22149875). CLEOPATRA demonstrated that first-line pertuzumab + trastuzumab + docetaxel, compared with placebo + trastuzumab + docetaxel, improved median PFS (HR = 0.62; p < 0.0001; 18.5 mo. vs. 12.4 mo.; no. of events, 47.5% (191/402) vs. 59.6% (242/406)) in patients with metastatic, HER2-Positive BCa. Secondary endpoints were OS (HR = 0.68), ORR (80.2% (275/343) vs. 69.3% (233/336)) and median DOR (20.2 mo. vs. 12.5 mo.).
pertuzumab/trastuzumab /hyaluronidase	FDA approved with paclitaxel for HER2-positive metastatic breast cancer that has not received prior anti-HER2 therapy or chemotherapy for metastatic disease. Per NCCN, pertuzumab/trastuzumab/hyaluronidase injection for subcutaneous use may be substituted anywhere that the combination of intravenous pertuzumab and intravenous trastuzumab are given as part of systemic therapy.	In a Phase III trial (FeDeriCa) that supported FDA approval, Phesgo (pertuzumab/trastuzumab/hyaluronidase-zzxf) demonstrated pharmacokinetics, safety, and efficacy comparable to i.v. pertuzumab and trastuzumab (H+P) (Cancer Res 2020;80(4 Suppl):Abstract nr PD4-07; NCT03493854), warranted the extrapolation of data from a Phase III trial supporting the approval of H+P plus docetaxel in Erbb2 (Her2)-positive metastatic breast cancer (PMID: 23602601; NCT00567190) for approval of Phesgo (FDA.gov).
trastuzumab + tucatinib + capecitabine	FDA approved for advanced unresectable or metastatic HER2-positive breast cancer, including brain metastases, that had one or more prior anti-HER2-based regimens in the metastatic setting. NCCN recommended as Category 1 /Preferred intervention.	In a Phase II trial (HER2CLIMB) that supported FDA approval, addition of Tukysa (tucatinib) to Herceptin (trastuzumab) and Xeloda (capecitabine) significantly improved progression-free survival at 1 year (PFS1) compared to placebo (33.1% vs 12.3%, HR=0.54, p<0.001) in patients with metastatic ERBB2 (HER2)-positive breast cancer who received prior HER2-targeted therapy, PFS1 was significantly improved (24.9% vs 0%, HR=0.48, p<0.001) in patients with brain metastasis (PMID: 31825569; NCT02614794).
trastuzumab +/- chemotherapy	FDA approved for HER2-overexpressing metastatic breast cancer, with paclitaxel as first-line treatment, and as a single agent after one or more chemotherapy regimens. NCCN recommended with various chemotherapy options as Category 2A.	The FDA approval for trastuzumab +/- chemotherapy was supported by two trials: Study 5 (PMID:11248153) and Study 6. Data from the open-label, randomized, phase-III trial Study 5 demonstrated that first-line trastuzumab + chemotherapy, compared with chemotherapy, improved median time to progression (p < 0.0001; 7.2 mo. vs. 4.5 mo.) in patients with metastatic, HER2-Positive BCa. Secondary endpoints were ORR (45% vs. 29%), median DOR (8.3 mo. vs 5.8. mo.), and median OS (25.1 mo. vs. 20.3 mo.). Data from the open-label, single-arm, phase-II trial Study 6 demonstrated that subsequent-line trastuzumab conferred an ORR of 14 % (CR, 2%; PR, 12%) in patients with metastatic, HER2-Positive BCa.
trastuzumab/hyaluronidase	FDA approved for HER2-overexpressing metastatic breast cancer, with paclitaxel as first-line treatment, and as a single agent after one or more chemotherapy regimens. Per NCCN, trastuzumab/hyaluronidase injection for subcutaneous use may be substituted for trastuzumab in any regimen.	The FDA approval for trastuzumab/hyaluronidase +/- chemotherapy was supported by two trials: H0648g (PMID: 11248153) and H0649g. Data from the open-label, randomized, phase-III trial H0648g demonstrated that first-line trastuzumab + chemotherapy, compared with chemotherapy, improved median time to progression (p < 0.0001; 7.2 mo. vs. 4.5 mo.) in patients with metastatic, HER2-Positive BCa. Secondary endpoints were ORR (45% vs. 29%), median DOR (8.3 mo. vs 5.8. mo.), and median OS (25.1 mo. vs. 20.3 mo.). Data from the open-label, single arm phase-II trial H0649g demonstrated that subsequent-line trastuzumab conferred an ORR of 14 % (CR, 2%; PR, 12%) in patients with metastatic, HER2-Positive BCa.

## TEST DETAILS

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PANEL CONTENT AND REPORTING TRANSCRIPTS				
ABL1 NM_005157.4 ^	DNAJB1 NM_006145.1	H2BC5 NM_021063.3	MYC NM_002467.4 +	COP1 NM_022457.5
ABL2 NM_007314.3	DNMT1 NM_001130823.1	H3C1 NM_003529.2	MYCL NM_001033082.2 +	RHEB NM_005614.3
ACVR1 NM_001105.4	DNMT3A NM_022552.4	H3C2 NM_003537.3	MYCN NM_005378.4 +	RHOA NM_001664.2
ACVR1B NM_020328.3	DNMT3B NM_006892.3	H3C3 NM_003531.2 +	MYD88 NM_002468.4 +	RICTOR NM_152756.3 +
AKT1 NM_001014432.1 +	DOT1L NM_032482.2	H3C4 NM_003530.4	MYOD1 NM_002478.4	RIT1 NM_006912.5
AKT2 NM_001626.4 +	E2F3 NM_001949.4	H3C6 NM_003532.2	NAB2 NM_005967.3 ^	RNF43 NM_017763.4
AKT3 NM_005465.4	EED NM_003797.3	H3C7 NM_021018.2	NBN NM_002485.4	ROS1 NM_002944.2 ^
ALK NM_004304.4 ^+	EGFL7 NM_016215.4	H3C8 NM_003534.2	NCOA3 NM_181659.2	RPS6KA4 NM_003942.2
ANKRD11 NM_001256182.1	EGFR NM_005228.3 ^+	H3C10 NM_003536.2	NCOR1 NM_006311.3	RPS6KB1 NM_003161.3 +
ANKRD26 NM_014915.2	EIF1AX NM_001412.3	H3C11 NM_003533.2	NEGR1 NM_173808.2	RPS6KB2 NM_003952.2
APC NM_000038.5 +	EIF4A2 NM_001967.3	H3C12 NM_003535.2	NF1 NM_001042492.2 +	RPTOR NM_020761.2
AR NM_000044.3 +	EIF4E NM_001130679.1	H3C15 NM_001005464.2	NF2 NM_000268.3 +	RUNX1 NM_001754.4
ARAF NM_001654.4	EML4 NM_019063.3	H3C14 NM_021059.2	NFE2L2 NM_006164.4 +	RUNX1T1 NM_175635.2
ARFRP1 NM_003224.4	EP300 NM_001429.3	H3C13 NM_001123375.2	NFKBIA NM_020529.2	RYBP NM_012234.5
	EPCAM NM_002354.2	H3-4 NM_003493.2		SDHA NM_004168.2
	EPHA3 NM_005233.5	HLA-A NM_002116.7		SDHAF2 NM_017841.2

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ARID1A NM_006015.4	EPHA5 NM_004439.5	HLA-B NM_005514.6	NKX2-1 NM_001079668.2	SDHB NM_003000.2
ARID1B NM_020732.3	EPHA7 NM_004440.3	HLA-C NM_002117.5	NKX3-1 NM_006167.3	SDHC NM_003001.3
ARID2 NM_152641.2	EPHB1 NM_004441.4	HNF1A NM_000545.5	NOTCH1 NM_017617.3	SDHD NM_003002.3
ARID5B NM_032199.2	ERBB2 NM_004448.2 <sup>+</sup>	HNRNPB NM_002140.3	NOTCH2 NM_024408.3	SETBP1 NM_015559.2
ASXL1 NM_015338.5	ERBB3 NM_001982.3 <sup>+</sup>	HOXB13 NM_006361.5	NOTCH3 NM_000435.2	SETD2 NM_014159.6 <sup>+</sup>
ASXL2 NM_018263.4	ERBB4 NM_005235.2 <sup>+</sup>	HRAS NM_005343.2 <sup>+</sup>	NOTCH4 NM_004557.3	SF3B1 NM_012433.2
ATM NM_000051.3 <sup>+</sup>	ERCC1 NM_001983.3 <sup>+</sup>	HSD3B1 NM_000862.2	NPM1 NM_002520.6	SH2B3 NM_005475.2
ATR NM_001184.3	ERCC2 NM_000400.3 <sup>+</sup>	HSP90AA1 NM_001017963.2	NRAS NM_002524.4 <sup>+</sup>	SH2D1A NM_002351.4
ATRX NM_000489.3 <sup>+</sup>	ERCC3 NM_000122.1	ICOSLG NM_015259.4	NRG1 NM_013964.3 <sup>+</sup>	SHQ1 NM_018130.2
AURKA NM_198433.1	ERCC4 NM_005236.2 <sup>+</sup>	ID3 NM_002167.4	NSD1 NM_002455.4	SLIT2 NM_004787.1
AURKB NM_004217.3	ERCC5 NM_000123.3	IDH1 NM_005896.2 <sup>+</sup>	NTRK1 NM_002529.3 <sup>^</sup>	SLX4 NM_032444.2
AXIN1 NM_003502.3	ERG NM_001136154.1	IDH2 NM_002168.2 <sup>+</sup>	NTRK2 NM_006180.3 <sup>^</sup>	SMAD2 NM_005901.5
AXIN2 NM_004655.3	ERRF1 NM_018948.3	IGF1 NM_001111283.1	NTRK3 NM_001012338.2	SMAD3 NM_005902.3
AXL NM_021913.4	ESR1 NM_001122742.1 <sup>+</sup>	IGF1R NM_000875.3	NUP93 NM_014669.4 <sup>^</sup>	SMAD4 NM_005359.5 <sup>+</sup>
B2M NM_004048.2	ETS1 NM_001143820.1 <sup>^</sup>	IGF2 NM_001127598.1	NUTM1 NM_175741.1 <sup>^</sup>	SMARCA4 NM_001128849.1 <sup>+</sup>
BAP1 NM_004656.3	ETV1 NM_004956.4 <sup>^</sup>	IKBKE NM_014002.3	PAK1 NM_001128620.1	SMARCB1 NM_003073.3 <sup>+</sup>
BARD1 NM_000465.2	ETV4 NM_001079675.2 <sup>^</sup>	IKZF1 NM_006060.4	PAK3 NM_002578.3	SMARCD1 NM_003076.4
BBC3 NM_001127240.2	ETV5 NM_004454.2 <sup>^</sup>	IL10 NM_000572.2	PAK5 NM_020341.3	SMC1A NM_006306.3
BCL10 NM_003921.4	ETV6 NM_001987.4 <sup>^</sup>	IL7R NM_002185.3	PALB2 NM_024675.3	SMC3 NM_005445.3
BCL2 NM_000633.2	EWSR1 NM_013986.3 <sup>^</sup>	INHA NM_002191.3	PRKN NM_004562.2	SMO NM_005631.4 <sup>+</sup>
BCL2L1 NM_138578.1	EZH2 NM_004456.4	INHBA NM_002192.2	PARP1 NM_001618.3	SNCAIP NM_005460.2
BCL2L11 NM_001204108.1	AMER1 NM_152424.3	INPP4A NM_001134224.1	PAX3 NM_181457.3 <sup>^</sup>	SOCS1 NM_003745.1
BCL2L2 NM_001199839.1	ABRAXAS1 NM_139076.2	INPP4B NM_003866.2	PAX5 NM_016734.2	SOX10 NM_006941.3
BCL6 NM_001706.4	TENT5C NM_017709.3	INSR NM_000208.2	PAX7 NM_001135254.1 <sup>^</sup>	SOX17 NM_022454.3
BCOR NM_001123385.1	FANCA NM_000135.2	IRF2 NM_002199.3	PAX8 NM_013953.3	SOX2 NM_003106.3
BCORL1 NM_021946.4	FANCC NM_000136.2	IRF4 NM_002460.3	PBRM1 NM_018313.4	SOX9 NM_000346.3
BCR NM_004327.3	FANCD2 NM_033084.3	IRS1 NM_005544.2	PDCD1 NM_005018.2	SPEN NM_015001.2
BIRC3 NM_001165.4	FANCE NM_021922.2	IRS2 NM_003749.2	PDCD1LG2 NM_025239.3	SPOP NM_001007228.1
BLM NM_000057.2	FANCF NM_022725.3	JAK1 NM_002227.2	PDGFRA NM_006206.4 <sup>+</sup>	SPTA1 NM_003126.2
BMPR1A NM_004329.2	FANCG NM_004629.1	JAK2 NM_004972.3 <sup>+</sup>	PDGFRB NM_002609.3 <sup>+</sup>	SRC NM_198291.2
BRAF NM_004333.4 <sup>^</sup>	FANCI NM_001113378.1	JAK3 NM_000215.3	PDK1 NM_001278549.1	SRSF2 NM_003016.4
BRCA1 NM_007294.3 <sup>+</sup>	FANCL NM_001114636.1	JUN NM_002228.3	PDK1 NM_001278549.1	STAG1 NM_005862.2
BRCA2 NM_000059.3 <sup>+</sup>	FAS NM_000043.4	KAT6A NM_006766.3	PDPK1 NM_002613.4	STAG2 NM_001042749.1
BRD4 NM_058243.2	FAT1 NM_005245.3	KDM5A NM_001042603.1	PGR NM_000926.4	STAT3 NM_139276.2
BRIP1 NM_032043.2	FBXW7 NM_033632.3 <sup>+</sup>	KDM5C NM_004187.3	PHF6 NM_032458.2	STAT4 NM_003151.3
BTG1 NM_001731.2	FGF1 NM_001144934.1 <sup>+</sup>	KDM6A NM_021140.2	PHOX2B NM_003924.3	STAT5A NM_003152.3
BTK NM_000061.2	FGF10 NM_004465.1 <sup>+</sup>	KDR NM_002253.2	PIK3C2B NM_002646.3	STAT5B NM_012448.3
EMSY NM_020193.3	FGF14 NM_175929.2 <sup>+</sup>	KEAP1 NM_012289.3	PIK3C2G NM_004570.4	STK11 NM_000455.4
CALR NM_004343.3	FGF19 NM_005117.2 <sup>+</sup>	KEL NM_000420.2	PIK3C3 NM_002647.2	STK40 NM_032017.1
CARD11 NM_032415.4	FGF2 NM_002006.4 <sup>+</sup>	KIF5B NM_004521.2	PIK3CA NM_006218.2 <sup>+</sup>	SUFU NM_016169.3 <sup>+</sup>
CASP8 NM_001228.4	FGF23 NM_020638.2 <sup>+</sup>	KIT NM_000222.2 <sup>+</sup>	PIK3CB NM_006219.2 <sup>+</sup>	SUZ12 NM_015355.2
CBFB NM_001755.2	FGF3 NM_005247.2 <sup>+</sup>	KLFL6 NM_130446.2	PIK3CD NM_005026.3	SYK NM_003177.5
CBL NM_005188.3	FGF4 NM_002007.2 <sup>+</sup>	KMT2B NM_014727.1	PIK3CG NM_002649.2	TBX3 NM_016569.3
CCND1 NM_053056.2 <sup>+</sup>	FGF5 NM_004464.3 <sup>+</sup>	KMT2C NM_170606.2	PIK3R1 NM_181523.2	ELOC NM_005648.3
CCND2 NM_001759.3	FGF6 NM_020996.1 <sup>+</sup>	KMT2D NM_003482.3	PIK3R2 NM_005027.3	TCF3 NM_003200.3
CCND3 NM_001760.3 <sup>+</sup>	FGF7 NM_002009.3 <sup>+</sup>	KRAS NM_004985.3 <sup>+</sup>	PIK3R3 NM_003629.3	TCF7L2 NM_030756.4
CCNE1 NM_001238.2 <sup>+</sup>	FGF8 NM_033163.3 <sup>+</sup>	LAMP1 NM_005561.3 <sup>+</sup>	PIM1 NM_002648.3	TERC
CD274 NM_014143.3	FGF9 NM_002010.2 <sup>+</sup>	LATS1 NM_004690.3	PLCG2 NM_002661.3	TERT NM_198253.2 <sup>+</sup>
CD276 NM_001024736.1	FGFR1 NM_023110.2 <sup>+</sup>	LATS2 NM_014572.2	PLK2 NM_006622.3	TET1 NM_030625.2
CD74 NM_001025159.2 <sup>^</sup>	FGFR2 NM_000141.4 <sup>^</sup>	LMO1 NM_002315.2	PMAIP1 NM_021127.2	TET2 NM_001127208.2
CD79A NM_001783.3	FGFR3 NM_000142.4 <sup>^</sup>	LRP1B NM_018557.2	PMS1 NM_000534.4	TFE3 NM_006521.4 <sup>^</sup>
CD79B NM_000626.2 <sup>+</sup>	FGFR4 NM_213647.1 <sup>+</sup>	LYN NM_002350.3	PMS2 NM_000535.5	TFRC NM_003234.2 <sup>+</sup>
CDC73 NM_024529.4	FH NM_000143.3	LZTR1 NM_006767.3	PNRC1 NM_006813.2	TGFBF1 NM_004612.2
CDH1 NM_004360.3 <sup>+</sup>	FLCN NM_144997.5	MAGI2 NM_012301.3	POLD1 NM_001256849.1	TGFBF2 NM_001024847.2
CDK12 NM_016507.2	FLI1 NM_002017.4	MALT1 NM_006785.3	POLE NM_006231.2	TMEM127 NM_017849.3
CDK4 NM_000075.3 <sup>+</sup>	FLT1 NM_002019.4	MAP2K1 NM_002755.3	PPARG NM_138712.3 <sup>^</sup>	TMPRSS2 NM_001135099.1 <sup>^</sup>
CDK6 NM_001259.6 <sup>+</sup>		MAP2K2 NM_030662.3	PPM1D NM_003620.3	TNFAIP3 NM_006290.3
CDK8 NM_001260.1		MAP2K4 NM_003010.3	PPP2R1A NM_014225.5	TNFRSF14 NM_003820.2
CDKN1A NM_000389.4		MAP3K1 NM_005921.1	PPP2R2A NM_001177591.1	TOP1 NM_003286.2
CDKN1B NM_004064.3		MAP3K13 NM_004721.4	PPP6C NM_001123355.1	TOP2A NM_001067.3
CDKN2A NM_000077.4 <sup>+</sup>		MAP3K14 NM_003954.3	PRDM1 NM_001198.3	TP53 NM_000546.5 <sup>+</sup>
		MAP3K4 NM_005922.2	PREX2 NM_024870.2	TP63 NM_003722.4
		MAPK1 NM_002745.4	PRKAR1A NM_212472.2	TRAF2 NM_021138.3

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CDKN2B NM_004936.3 <sup>+</sup>	FLT3 NM_004119.2	MAPK3 NM_002746.2	PRKCI NM_002740.5	TRAF7 NM_032271.2 <sup>+</sup>
CDKN2C NM_001262.2	FLT4 NM_182925.4	MAX NM_002382.4	PRKDC NM_006904.6	TSC1 NM_000368.4
CEBPA NM_004364.3	FOXA1 NM_004496.3	MCL1 NM_021960.4	PRSS8 NM_002773.3	TSC2 NM_000548.3
CENPA NM_001809.3	FOXL2 NM_023067.3	MDC1 NM_014641.2	PTCH1 NM_000264.3 <sup>+</sup>	TSHR NM_000369.2
CHD2 NM_001271.3	FOXO1 NM_002015.3	MDM2 NM_002392.5 <sup>+</sup>	PTEN NM_000314.4 <sup>+</sup>	U2AF1 NM_006758.2
CHD4 NM_001273.2	FOXP1 NM_032682.5	MDM4 NM_002393.4 <sup>+</sup>	PTPN11 NM_002834.3	VEGFA NM_001025366.2
CHEK1 NM_001114122.2 <sup>+</sup>	FRS2 NM_001278351.1	MED12 NM_005120.2	PTPRD NM_002839.3	VHL NM_000551.3 <sup>+</sup>
CHEK2 NM_007194.3 <sup>+</sup>	FUBP1 NM_003902.3 <sup>+</sup>	MEF2B NM_001145785.1	PTPRS NM_002850.3	VTCN1 NM_024626.3
CIC NM_015125.3 <sup>+</sup>	FYN NM_002037.5	MEN1 NM_130799.2	PTPRT NM_133170.3	CCN6 NM_003880.3
CREBBP NM_004380.2	GABRA6 NM_000811.2	MET NM_000245.2 <sup>+</sup>	QKI NM_006775.2	WT1 NM_024426.4
CRKL NM_005207.3	GATA1 NM_002049.3	MGA NM_001164273.1	RAB35 NM_006861.6	XIAP NM_001167.3
CRLF2 NM_022148.2	GATA2 NM_032638.4	MITF NM_000248.3	RAC1 NM_018890.3	XPO1 NM_003400.3
CSF1R NM_005211.3	GATA3 NM_001002295.1 <sup>+</sup>	MLH1 NM_000249.3	RAD21 NM_006265.2	XRCC2 NM_005431.1
CSF3R NM_156039.3	GATA4 NM_002052.3	KMT2A NM_001197104.1	RAD50 NM_005732.3	YAP1 NM_001130145.2
CSNK1A1 NM_001025105.2	GATA6 NM_005257.4	MLL3 NM_004529.2	RAD51 NM_002875.4	YES1 NM_005433.3
CTCF NM_006565.3	GEN1 NM_182625.3	MPL NM_005373.2	RAD51B NM_133509.3	ZBTB2 NM_020861.1
CTLA4 NM_005214.4	GID4 NM_024052.4	MRE11 NM_005591.3	RAD51C NM_058216.2	ZBTB7A NM_015898.2
CTNNA1 NM_001903.2	GLI1 NM_005269.2	MSH2 NM_000251.2	RAD51D NM_002878.3	ZFH3 NM_006885.3
CTNNA1 NM_001903.2	GNA11 NM_002067.2	MSH3 NM_002439.4	RAD52 NM_134424.2	ZNF217 NM_006526.2
CTNNA1 NM_001903.2	GNA13 NM_006572.4	MSH6 NM_000179.2	RAD54L NM_001142548.1	ZNF703 NM_025069.1
CUL3 NM_003590.4	GNAQ NM_002072.3	MST1 NM_020998.3	RAF1 NM_002880.3 <sup>+</sup>	ZRSR2 NM_005089.3
CUX1 NM_181552.3	GNAS NM_000516.4 <sup>+</sup>	MST1R NM_002447.2	RANBP2 NM_006267.4	MTAP NM_002451.3 <sup>+</sup> *
CXCR4 NM_003467.2	ADGRA2 NM_032777.9	MTOR NM_004958.3	RARA NM_000964.3	
CYLD NM_015247.2	GPS2 NM_004489.4	MUTYH NM_001128425.1	RASA1 NM_002890.2	
DAXX NM_001141970.1	GREM1 NM_013372.6	MYB NM_001130173.1	RB1 NM_000321.2 <sup>+</sup>	
DCUN1D1 NM_0020640.2	GRIN2A NM_000833.3		RBM10 NM_005676.4	
DDR2 NM_001014796.1	GRM3 NM_000840.2		RECQL4 NM_004260.3	
DDX41 NM_016222.2	GSK3B NM_002093.3		REL NM_002908.2	
DHX15 NM_001358.2	H3-3A NM_002107.4 <sup>+</sup>		RET NM_020975.4 <sup>^+</sup>	
DICER1 NM_177438.2	H3-3B NM_005324.3			
DJS3 NM_014953.3	H3-5 NM_001013699.2			
	HGF NM_000601.4			
	H1-2 NM_005319.3			

<sup>^</sup>Summit™ also reports fusion events for this gene  
<sup>+</sup>Summit™ also reports copy number alterations for this gene  
<sup>\*</sup>Summit™ only reports copy number alterations for this gene

## Methods and Limitations

The Summit™ 2.0 comprehensive genomic profiling (CGP) next-generation sequencing (NGS) test investigates tumor derived nucleic acid extracted from cerebrospinal fluid (CSF) for clinically relevant single/multi nucleotide variants (SNVs, MNVs), insertions and deletions (indels), gene level copy number variants (CNVs), and other biomarkers such as tumor mutation burden (TMB) and microsatellite instability (MSI). Methodology involves evaluation of 520 genes for SNVs, MNVs, Indels, 62 genes for CNVs, 28 genes for fusions, as well as TMB and MSI (PMID: 41595175). The LOD (limit of detection) for SNVs, MNVs and Indels was determined to be 0.3% variant allelic frequency (VAF), for CNVs was determined to be  $\geq 2$ -fold change for amplifications and  $\leq 0.5$ -fold change for deletions, and for fusions was determined to be  $\geq 2$  supporting reads. Reporting thresholds for TMB and MSI are:  $< 10$  Mut/Mb (TMB low),  $\geq 10$  Mut/Mb (TMB high), and when total unstable sites are  $< 30\%$  (MSS) and  $\geq 30\%$  (MSI-High). Variants are called against the human genome build reference hg19 using Summit™ Omics pipeline version 1.3.0, developed at Belay Diagnostics.

Tertiary analysis is performed using the precision oncology workbench (GenomOncology) based on the joint AMP/ASCO/CAP consensus guidelines for interpretation of sequence variants in cancer (PMID: 27993330). Please reach out to contact@belaydiagnostics.com for additional information or queries.

## Disclaimers

This test was developed, and its performance characteristics determined by Belay Diagnostics Laboratory (CLIA# 14D2302605), which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity testing. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). This test may be used for clinical purposes. However, the results of this test do not establish a diagnosis and should not be used alone for diagnosis or patient care decisions or otherwise replace the judgment of a treating physician and must always be interpreted in the context of all relevant clinical and pathological data.

This test is performed only to evaluate for somatic (i.e., tumor-specific) variants within the genes listed and cannot distinguish between germline and somatic alterations with absolute certainty. This test therefore does not report on incidental findings as defined by the American College for Medical Genetics and Genomics (ACMG) (PMID: 37347242). If a germline variant is suspected, follow-up germline testing using non-neoplastic (normal) tissue

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should be performed by a laboratory permitted to perform germline genetic testing along with genetic counseling. It is possible for a genomic variant to be present yet go undetected by our assay either due to the heterogeneous nature of the specimen or the limits of detection of our assay. Therefore, to the extent a particular genomic variant is not reported, Belay Diagnostics LLC does not guarantee that the variant does not exist in the specimen provided. Likely benign, and benign variants are not reported. For any reported variant of uncertain significance (VUS), if the classification changes, there is no obligation to send out a new report updating this information.

The information presented in the clinical trials and therapeutic sections of this report is compiled from public sources which are continuously updated. While we strive to ensure this information is accurate and complete, we cannot guarantee the accuracy or completeness of this information. This public sourced information is not ranked in order of potential or predicted efficacy and may not be complete. Specific eligibility criteria should be reviewed as applicable. This information may include associations between a genomic variant (or lack of a variant) and one or more therapeutic agents with potential clinical benefit (or lack of clinical benefit), including agents that are being studied in clinical research. The finding of a genomic variant does not necessarily indicate or demonstrate pharmacologic effectiveness (or lack thereof) of any agent or treatment regimen found in public source information. Similarly, the finding of "no clinically significant variant" does not necessarily indicate or demonstrate lack of pharmacologic effectiveness (or lack of effectiveness) of any agent or treatment regimen found in public source information. Belay Diagnostics expressly disclaims, and makes no representation of or warranty of, the accuracy or completeness with respect to the publicly available information included herein or reviewed or collected during creation of this report.

### ACTIONABILITY REFERENCES

**FDA:** U.S. Food & Drug Administration ([fda.gov](http://fda.gov))

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**WHO:** World Health Organization Classification of Tumours online ([tumourclassification.iarc.who.int](http://tumourclassification.iarc.who.int))

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