Ambry Genetics
A Konica Minolta Company

SAMPLE REPORT

Ordered By	Contact ID:1374148 Org ID:1	Patient Name: **Last, First**	
Physician:	Unknown, Unknown, MD	Accession #: **00-055938**	Specimen #: 1234
	Ph:N/A Fx:N/A	AP2 Order #: 633474	Specimen: Blood EDTA (Purple top)
Client:	Ambry	Birthdate: 01/01/1976	Age: 43y 7m
	CA US	Gender: M	
Additional Authorized Recipient:		MRN #: N/A	Collected: 08/26/2019
Thai, Julia Ph:(949) 900-5500 Fx:(949) 900-5501		Indication: Diagnostic	Received: 08/27/2019
		Ethnicity: Caucasian	

CancerNext-Expanded +RNAinsight™: Analyses of 67 Genes Associated with Hereditary Cancer

RESULTS

CDH1 **Variant, Likely Pathogenic: p.E353K**

SUMMARY

POSITIVE: Likely Pathogenic Variant Detected

INTERPRETATION

- This individual is heterozygous for the **p.E353K** likely pathogenic variant in the *CDH1* gene.
- This result is consistent with a diagnosis of hereditary diffuse gastric cancer (HDGC) syndrome.
- **Risk estimate**: lifetime risks of 67-83% for diffuse gastric cancer and 39-52% for lobular breast cancer (females only).
- +RNAinsight data for this individual contributed to a clinically significant variant reclassification. See variant additional information below.
- The expression and severity of disease for this individual cannot be predicted.
- Genetic testing for likely pathogenic variants (VLPs) in family members can be helpful in identifying at-risk individuals.
- Genetic counseling is a recommended option for all individuals undergoing genetic testing.

No additional pathogenic mutations, variants of unknown significance, or gross deletions or duplications were detected. Genes Analyzed (67 total): ***AIP, ALK, APC*, ATM*, BAP1, BARD1, BLM, BMPR1A, BRCA1*, BRCA2*, BRIP1*, CDH1*, CDK4, CDKN1B, CDKN2A, CHEK2*, DICER1, FANCC, FH, FLCN, GALNT12, HOXB13, MAX, MEN1, MET, MLH1*, MRE11A, MSH2*, MSH6*, MUTYH*, NBN, NF1*, NF2, PALB2*, PHOX2B, PMS2*, POLD1, POLE, POT1, PRKAR1A, PTCH1, PTEN*, RAD50, RAD51C*, RAD51D*, RB1, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, SMARCB1, SMARCE1, STK11, SUFU, TMEM127, TP53*, TSC1, TSC2, VHL*** **and** ***XRCC2*** **(sequencing and deletion/duplication);** ***MITF*** **(sequencing only);** ***EPCAM*** **and** ***GREM1*** **(deletion/duplication only)**. DNA and RNA analyses performed for * genes.

CDH1 **Additional Information**

The **p.E353K** variant (also known as c.1057G>A), located in coding exon 8 of the *CDH1* gene, results from a G to A substitution at nucleotide position 1057. The glutamic acid at codon 353 is replaced by lysine, an amino acid with similar properties. This alteration has been detected in two individuals whose personal and/or family histories are consistent with *CDH1*-associated hereditary cancer syndrome (Ambry internal data). Using the BDGP and ESEfinder splice site prediction tools, this alteration is predicted to create a new alternate splice donor site. This prediction was supported in RNA studies demonstrating abnormal splicing in the set of samples tested (Ambry internal data). This variant was not reported in population-based cohorts in the Genome Aggregation Database (gnomAD) (Lek M et al. *Nature.* 2016 08;536:285-91). Based on the majority of available evidence to date, this variant is likely to be pathogenic.

The *CDH1* tumor suppressor gene (NM_004360.3) encodes the E-cadherin protein, which is involved in cell-to-cell adhesion, signal

transmission, and cellular migration. Germline *CDH1* mutations are associated with hereditary diffuse gastric cancer (HDGC), an autosomal dominant cancer predisposition syndrome characterized by significantly elevated risks of multiple malignancies. Monoallelic pathogenic *CDH1* mutations are estimated confer a 67-83% lifetime risk of diffuse gastric cancer, and female carriers also have a 39-52% lifetime risk of lobular breast cancer (Pharoah PD et al. *Gastroenterology*. 2001 Dec;121(6):1348-53; Kaurah P et al. *JAMA*. 2007 Jun 6;297(21):2360-72). Breast cancer risk estimates for male *CDH1* mutation carriers are not currently available.

Order Summary: The following products were included in the test order for this individual. Please note: tests on hold and those that have been cancelled (including reflex testing steps cancelled due to a positive result in a preceding test) are excluded. For additional information, please contact Ambry Genetics.

- CancerNext-Expanded +RNAinsight™ (Product Code 8874-R)

ASSAY INFORMATION

Methodology: The **CancerNext-*Expanded* +RNAinsight™** test is a comprehensive screen of 67 genes associated with hereditary cancer predisposition. Genomic deoxyribonucleic acid (gDNA) and ribonucleic acid (RNA) are isolated from the patient's specimen using standardized methodology and quantified. RNA is converted to complementary DNA (cDNA) by reverse transcriptase polymerase chain reaction (RT-PCR). Sequence enrichment of the targeted coding exons and adjacent intronic nucleotides is carried out by a bait-capture methodology using long biotinylated oligonucleotide probes followed by polymerase chain reaction (PCR) and Next-Generation sequencing. Additional DNA analyses include Sanger sequencing for any regions missing or with insufficient read depth coverage for reliable heterozygous variant detection. Reportable small insertions and deletions, potentially homozygous variants, variants in regions complicated by pseudogene interference, and single nucleotide variant calls not satisfying 100x depth of coverage and 40% het ratio thresholds are verified by Sanger sequencing (Mu W et al. *J Mol Diagn*. 2016 Oct 4. PubMed PMID: 27720647). For *BRCA2* and *MSH2*, the Portuguese founder mutation, c.156_157insAlu (also known as 384insAlu), and the coding exons 1-7 inversion, respectively, are detected by next generation sequencing and confirmed by multiplex ligation-dependent probe amplification (MLPA) or PCR and agarose gel electrophoresis. Gross deletion/duplication analysis for 65 of the genes (excluding *MITF* and *PMS2*) is performed using a custom pipeline based on read-depth from NGS data and/or targeted chromosomal microarray with confirmatory MLPA when applicable. Gross deletion/duplication analysis of *PMS2* is performed using MLPA kit P008-B1. If a deletion is detected in exons 13, 14, or 15 of *PMS2*, double stranded sequencing of the appropriate exon(s) of the pseudogene *PMS2CL* will be performed to determine if the deletion is located in the *PMS2* gene or pseudogene. All sequence analysis is based on the following NCBI reference sequences: *AIP*- NM_003977.2, *ALK*- NM_004304.4, *APC*- NM_000038.5 & NM_001127511.2, *ATM*- NM_000051.3, *BAP1*- NM_004656.2, *BARD1*- NM_000465.2, *BLM*- NM_000057.2, *BMPR1A*- NM_004329.2, *BRCA1*- NM_007294.3, *BRCA2*- NM_000059.3, *BRIP1*- NM_032043.2, *CDH1*- NM_004360.3, *CDK4*- NM_000075.3, *CDKN1B*- NM_004064.3, *CDKN2A*- NM_000077.4 and NM_058195.3 (p14ARF), *CHEK2*- NM_007194.3, *DICER1*-NM_177438.2, *FANCC*- NM_000136.2, *FH*- NM_000143.3, *FLCN*- NM_144997.5, *GALNT12*- NM_024642.4, *HOXB13*- NM_006361.5, *MAX*- NM_002382.3, *MEN1*- NM_130799.2, *MET*- NM_000245.1, *MITF*- NM_000248.3, *MUTYH*- NM_001128425.1, *MRE11A*- NM_005591.3, *MLH1*- NM_000249.3, *MSH2*- NM_000251.1, *MSH6*- NM_000179.2, *NBN*- NM_002485.4, *NF1*-NM_000267.3, *NF2*- NM_000268.3, *PALB2*- NM_024675.3, *PHOX2B*- NM_003924.3, *PMS2*- NM_000535.5, *POLD1*- NM_002691.2, *POLE*- NM_006231.2, *POT1*-NM_015450.2, *PRKAR1A*- NM_002734.3, *PTCH1*- NM_000264.3, *PTEN*- NM_000314.4, *RAD50*- NM_005732.3, *RAD51C*- NM_058216.1, *RAD51D*- NM_002878.3, *RB1*- NM_000321.2, *RET*- NM_020975.4, *SDHA*- NM_004168.2, *SDHAF2*- NM_017841.2, *SDHB*- NM_003000.2, *SDHC*- NM_003001.3, *SDHD*- NM_003002.2, *SMAD4*- NM_005359.5, *SMARCA4*- NM_001128849.1, *SMARCB1*- NM_003073.3, *SMARCE1*- NM_002079.4, *STK11*- NM_000455.4, *SUFU*- NM_016169.3, *TMEM127*- NM_017849.3, *TP53*- NM_000546.4, *TSC1*- NM_000368.4, *TSC2*- NM_000548.3, *VHL*- NM_000551.3, *XRCC2*- NM_005431.1.

Analytical Range: The **CancerNext-*Expanded* +RNAinsight™** test targets detection of DNA sequence mutations in 65 genes by either Next-Generation or Sanger sequencing of all coding domains and well into the flanking 5' and 3' ends of all the introns and untranslated regions. In addition, sequencing of the promoter region is performed for the following genes: *PTEN* (c.-1300 to c.-745), *MLH1* (c.-337 to c.-194), and *MSH2* (c.-318 to c.-65). For *MITF*, only the status of the c.952G>A (p.E318K) alteration is analyzed and reported. For *POLD1* and *POLE,* missense variants located outside of the exonuclease domains (codons 311-541 and 269-485, respectively) are not routinely reported. For *ALK*, only variants located within the kinase domain (c.3286-c.4149) are reported. For *PHOX2B*, the polyalanine repeat region is excluded from analysis. Gross deletion/duplication analysis determines gene copy number for the covered exons and untranslated regions for 64 of the 65 sequenced genes (excluding *MITF*), *EPCAM,* and *GREM1*. For *GREM1,* only the status of the 40kb 5'UTR gross duplication is analyzed and reported. For *EPCAM*, only gross deletions encompassing the 3' end of the gene are reported. For *APC*, all promoter 1B gross deletions as well as single nucleotide substitutions within the promoter 1B YY1 binding motif (NM_001127511 c.-196_-186) are analyzed and reported. RNA transcripts are screened for 18 genes (*APC, ATM, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, MLH1, MSH2, MSH6, MUTYH, NF1, PALB2, PMS2* exons 1-10, *PTEN, RAD51C, RAD51D*, and *TP53*) and compared to a human reference pool. The absence or presence of RNA transcripts meeting quality thresholds are incorporated as evidence towards assessment and classification of DNA variants. Any regions not meeting RNA quality thresholds are excluded from analysis. Regions routinely excluded due to chronically low expression in human peripheral lymphocytes include: *BRCA2* (exon 1), *BRIP1* (exons 18, 20), *CDH1* (Exons 1, 2, 16), and *CHEK2* (exons 1, 7, 8).

Result Reports: In result reports, DNA alterations in the following classifications are always reported, and are based on the following definitions:

- **Pathogenic Mutation**: alterations with sufficient evidence to classify as pathogenic (capable of causing disease). Previously described pathogenic mutations, including intronic mutations at any position, are always reported when detected.
- **Variant, Likely Pathogenic (VLP)**: alterations with strong evidence in favor of pathogenicity. Previously described likely pathogenic variants, including intronic VLPs at any position, are always reported when detected.
- **Variant, Unknown Significance (VUS)**: alterations with limited and/or conflicting evidence regarding pathogenicity. Intronic VUSs are always reported out to 5 basepairs from the splice junction when detected.

Alterations of unlikely clinical significance (those with strong/very strong evidence to argue against pathogenicity) are not routinely included on results reports. These include findings classified as "likely benign" and "benign" alterations.

Assay Information Continued on Next Page

ASSAY INFORMATION *(Supplement to Test Results - Continued)*

Resources: The following references are used in variant analysis and classification when applicable for observed genetic alterations.

1. The 1000 Genomes Project Consortium. An integrated map of genetic variation from 1092 human genomes. *Nature*. 2012;491:56-65.
2. ACMG Standards and guidelines for the interpretation of sequence variants. *Genet Med.* 2015 May;17(5):405-23.
3. Ambry Genetics Variant Classification Scheme. http://www.ambrygen.com/variant-classification.
4. Berkeley Drosophila Genome Project [Internet]. Reese MG et al. *J Comp Biol.* 1997;4:311-23. http://www.fruitfly.org/seq_tools/splice.html.
5. Database of Single Nucleotide Polymorphisms (dbSNP) [Internet]. Bethesda (MD): National Center for Biotechnology Information, National Library of Medicine (dbSNP Build ID:135) Available from: www.ncbi.nlm.nih.gov/SNP. Accessed Jan 2012).
6. ESEfinder [Internet]. Smith PJ, et al. (2006) *Hum Mol Genet.* 15(16):2490-2508 and Cartegni L, et al. *Nucleic Acid Research.* 2003;31(13):3568-3571. http://rulai.cshl.edu/cgi-bin/tools/ESE3/esefinder.cgi?process=home.
7. Exome Variant Server, NHLBI Exome Sequencing Project (ESP) [Internet], Seattle WA. Available from: evs.gs.washington.edu/EVS.
8. Grantham R. Amino acid difference formula to help explain protein evolution. *Science.* 1974;185(4151):862-864.
9. HGMD® [Internet]: Stenson PD et al. *Genome Med.* 2009;1(1):13. www.hgmd.cf.ac.uk.
10. Landrum MJ et al. ClinVar: public archive of relationships among sequence variation and human phenotype. *Nucleic Acids Res*. 2014 Jan 1;42(1):D980-5. doi: 10.1093/nar/gkt1113. PubMed PMID: 24234437.
11. Online Mendelian Inheritance in Man, OMIM®. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD), Copyright® 1966-2012. World Wide Web URL: http://omim.org.
12. Feng BJ. PERCH: A Unified Framework for Disease Gene Prioritization. *Hum Mutat.* 2017 Mar;38(3):243-251.
13. Exome Aggregation Consortium (ExAC) [Internet], Cambridge, MA. Available from: http://exac.broadinstitute.org.
14. Genome Aggregation Database (gnomAD) [Internet], Cambridge, MA. Available from: http://gnomad.broadinstitute.org.
15. Lek M et al. Analysis of protein-coding genetic variation in 60,706 humans. *Nature*. 2016 Aug 17;536(7616):285-91. PMID: 27535533

Disclaimer: This test was developed and its performance characteristics were determined by Ambry Genetics Corporation. It has not been cleared or approved by the US Food and Drug Administration. The FDA does not require this test to go through premarket FDA review. It should not be regarded as investigational or for research. This test should be interpreted in context with other clinical findings. This report does not represent medical advice. Any questions, suggestions, or concerns regarding interpretation of results should be forwarded to a genetic counselor, medical geneticist, or physician skilled in interpretation of the relevant medical literature. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. This test analyzes the following types of mutations: nucleotide substitutions, small deletions (up to 25 bp), small insertions (up to 10 bp), small indels and gross deletions/duplications. Unless otherwise noted in the methodology section above, it is not intended to analyze the following types of alterations: gross rearrangements, deep intronic variations, Alu element insertions, and other unknown abnormalities. The pattern of mutation types varies with the gene tested and this test detects a high but variable percentage of known and unknown mutants of the classes stated. A negative result from the analysis cannot rule out the possibility that the tested individual carries a rare unexamined mutation or mutation in the undetectable group. This test is designed and validated to be capable of detecting ~99% of described mutations in the 67 genes represented on the test (analytical sensitivity). The clinical sensitivity of this test may vary widely according to the specific clinical and family history. Cancer is a complex clinical disorder. Mutations in other genes or the regions not analyzed by this test can also give rise to similar clinical conditions. Although molecular tests are highly accurate, rare diagnostic errors may occur. Possible diagnostic errors include sample mix-up, erroneous paternity identification, technical errors, clerical errors, and genotyping errors. Genotyping errors can result from trace contamination of PCR reactions, from maternal cell contamination in fetal samples, from rare genetic variants that interfere with analysis, low-level mosaicism, presence of pseudogenes, technical difficulties in regions with high GC content or homopolymer tracts, presence of pre-malignant or malignant cells in the sample, or from other sources. Rare variants present in the human genome reference sequence (GRCh37.p5/hg19) or rare misalignment due to presence of pseudogenes can lead to misinterpretation of patient sequence data.

Ambry Genetics®
A Konica Minolta Company

Clinician Management Resource for *CDH1* (Hereditary diffuse gastric cancer)

This overview of clinical management guidelines is based on this patient's positive test result for a *CDH1* gene mutation. Unless otherwise stated, medical management guidelines used here are limited to those issued by the National Comprehensive Cancer Network® (NCCN®)[1,2] in the U.S. Please consult the referenced guideline for complete details and further information.

Clinical correlation with the patient's past medical history, treatments, surgeries and family history may lead to changes in clinical management decisions; therefore, other management recommendations may be considered. Genetic testing results and medical society guidelines help inform medical management decisions but do not constitute formal recommendations. Discussions of medical management decisions and individualized treatment plans should be made in consultation between each patient and his or her healthcare provider, and may change over time.

SCREENING/SURGICAL CONSIDERATIONS	AGE TO START	FREQUENCY
Gastric Cancer[1]		
Prophylactic gastrectomy is recommended. • Baseline endoscopy prior to gastrectomy • Intraoperative frozen sections should be performed to ensure complete removal of gastric tissue • A D2 lymph node dissection is not necessary • Not recommended under 18 years of age, but may be considered for certain patients (i.e. family history of gastric cancer diagnosed under age 25)	Between 18-40 years old	N/A
Patients who elect not to undergo prophylactic gastrectomy should be offered upper endoscopy with multiple random biopsies	Individualized	Every 6-12 months
Female Breast Cancer[2]		
Breast awareness • Women should be familiar with their breasts and promptly report changes to their healthcare provider.	18 years old	Periodic and consistent
Clinical Breast Exam	25 years old	Every 6-12 months
Breast Screening • Mammography with consideration of tomosynthesis • Consider breast MRI with contrast	30 years old, or 5-10 years before the earliest known breast cancer in the family	Every 12 months
For consideration of risk-reducing mastectomy , manage based on family history	Individualized	N/A
Consider investigational imaging and screening studies, when available in context of a clinical trial	Individualized	N/A
Consider options for risk reduction agents, such as chemoprevention (i.e. tamoxifen)	Individualized	N/A

1. NCCN Clinical Practice Guidelines in Oncology®. Gastric Cancer. V1.2018. Available at nccn.org.
2. NCCN Clinical Practice Guidelines in Oncology®. Genetic/Familial High-Risk Assessment: Breast and Ovarian. V1.2018. Available at nccn.org.
3. Rex DK, *et al.* American College of Gastroenterology guidelines for colorectal cancer screening. Am J. Gastroenterol. 2009 Mar;104(3):739-50.

Ambry Genetics®
A Konica Minolta Company

Clinician Management Resource for *CDH1* (Hereditary diffuse gastric cancer)

SCREENING/SURGICAL CONSIDERATIONS	AGE TO START	FREQUENCY
Colorectal Cancer[3]		
Colonoscopy *Alternate screening tests are available. Please reference the American College of Gastroenterology guidelines for further information.*	50 years old 45 years old for African Americans	Every 10 years

1. NCCN Clinical Practice Guidelines in Oncology®. Gastric Cancer. V1.2018. Available at nccn.org.
2. NCCN Clinical Practice Guidelines in Oncology®. Genetic/Familial High-Risk Assessment: Breast and Ovarian. V1.2018. Available at nccn.org.
3. Rex DK, *et al.* American College of Gastroenterology guidelines for colorectal cancer screening. Am J. Gastroenterol. 2009 Mar;104(3):739-50.

7 Argonaut, Aliso Viejo, CA 92656 USA Toll Free +1 866 262 7943 Fax +1 949 900 5501 ambrygen.com

Ambry Genetics

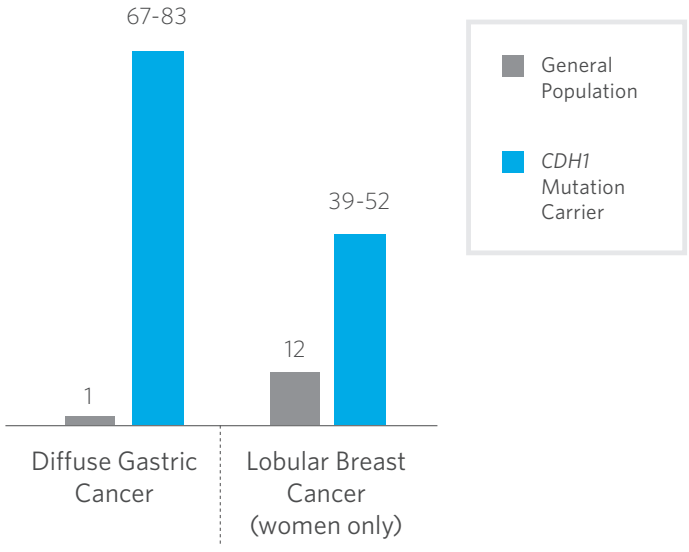
Understanding Your Positive *CDH1* Genetic Test Result

INFORMATION FOR PATIENTS WITH A **PATHOGENIC MUTATION** OR **VARIANT, LIKELY PATHOGENIC**

5 Things To Know

1	*CDH1* mutation	Your testing shows that you have a pathogenic mutation or a variant that is likely pathogenic in the *CDH1* gene.
2	Hereditary diffuse gastric cancer (HDGC)	People with *CDH1* mutations have hereditary diffuse gastric cancer (HDGC).
3	Cancer risks	You have an increased chance to develop a particular type of gastric cancer (diffuse) and a particular type of female breast cancer (lobular).
4	What you can do	There are risk management options to detect cancer early or lower the risk to develop cancer. It is important to discuss these options with your doctor, and decide on a plan that best manages cancer risks.
5	Family	Family members may also be at risk – they can be tested for the *CDH1* mutation that was identified in you.

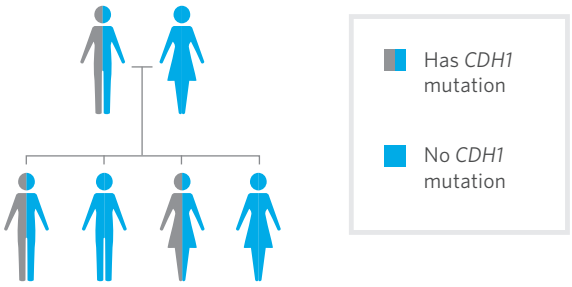
CDH1 Cancer Risks to Age 80 (%)*



**The above cancer risks represent the typical range for individuals with a mutation in this gene. If available, cancer risks specific to the mutation found in you will be provided in your results report.*

CDH1 Mutations in the Family

There is a 50/50 random chance to pass on a *CDH1* mutation to your sons and daughters. The image below shows that both men and women can carry and pass on these mutations.



Understanding Your Positive *CDH1* Genetic Test Result

INFORMATION FOR PATIENTS WITH A **PATHOGENIC MUTATION** OR **VARIANT, LIKELY PATHOGENIC**

Result	**MUTATION**	Your testing shows that you have a pathogenic mutation (a disease-causing change in the gene, like a spelling mistake) or a variant that is likely pathogenic in the *CDH1* gene. Both of these results should be considered positive.
Gene	***CDH1***	Everyone has two copies of the *CDH1* gene, which we randomly inherit from each of our parents. Mutations in one copy of the *CDH1* gene can increase the chance for you to develop certain types of cancer in your lifetime.
Condition	**HDGC**	People with *CDH1* mutations have hereditary diffuse gastric cancer (HDGC).
Cancer Risks	**INCREASED**	You have an increased chance to develop a particular type of gastric cancer (diffuse) and a particular type of female breast cancer (lobular).
Management Options	**FOR WOMEN**	Options for early detection and prevention for women may include: breast exam, mammogram, breast MRI, and options for preventive surgery. Talk to your doctor about what options may be right for you.
Management Options	**FOR MEN & WOMEN**	Options for early detection and prevention for men and women may include: upper endoscopy with random biopsies, options for preventive surgery, or other screening tools. Talk to your doctor about what options may be right for you.
Risk Management	**VARIES**	Risk management decisions are very personal, and the best option depends on many factors. Screening typically begins earlier than the general population and is often more frequently performed. It is important to discuss these options with your doctor.
Family Members	**50/50 CHANCE**	Your close relatives (like your parents, brothers, sisters, children) have a 50/50 random chance of inheriting the *CDH1* mutation that you carry, and other family members (aunts, uncles, cousins) may also inherit it. Your relatives can be tested for this same mutation. Depending on the family history, those who DO NOT have it may not have an increased chance (above the general population) to develop cancer.
Next Steps	**DISCUSS**	It is recommended that you share this information with family members so they can learn more and discuss this with their healthcare providers.
Reach Out	**RESOURCES**	• Ambry's Hereditary Cancer Site for Families patients.ambrygen.com/cancer • No Stomach for Cancer nostomachforcancer.org • Genetic Information Nondiscrimination Act (GINA) ginahelp.org • National Society of Genetic Counselors nsgc.org • Canadian Society of Genetic Counsellors cagc-accg.ca

Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your *CDH1* result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or interpreted as medical advice.

7 Argonaut, Aliso Viejo, CA 92656 USA Toll Free +1.866.262.7943 Fax +1.949.900.5501 ambrygen.com

Ambry Genetics®
A Konica Minolta Company

PROMPT
Prospective Registry Of MultiPlex Testing

Opportunity to Enroll in Hereditary Cancer Research

Genetic testing can help individuals and families by giving them a clearer idea of their cancer risks. Genetic tests (called multi-gene or multiplex panels) look for changes in several different genes, all in a single test. While all of the genes on these panels have been tied to an increased risk of cancer, we understand the risks associated with some of the genes better than we understand others. One way to help improve our understanding is to enroll people with pathogenic mutations or variants of unknown significance in registries. Registries typically follow people over many years to learn more about these alterations and how they impact their health.

How can I find a research registry?

There are several hereditary cancer research registries that are studying individuals who have had multi-gene panel testing. One registry that is open to individuals nationwide is PROMPT (or Prospective Registry Of MultiPlex Testing). PROMPT is an online registry for patients and families who have had multi-gene testing and have been found to have a genetic variation which may be linked to an increased risk of cancer. PROMPT is a joint effort involving several academic medical centers and commercial laboratories, working together to learn more about the genes that are studied on multi-gene panels. PROMPT will allow researchers to better understand the cancer risks associated with changes in these genes and thus provide a better understanding of the best way to take care of individuals who have such changes.

What is involved in participation?

Participation in the study simply involves completing online surveys. You can take part without providing any personal information to the PROMPT study. But, if you are interested, the PROMPT team will reach out to you to talk about ways that you can get more involved with the research effort. Either way, your participation will help researchers learn more and improve the ability of this genetic testing to help people.

How do I enroll?

You can learn more about or register for PROMPT by going to www.promptstudy.org
or by scanning the QR code to the right.

Thank you again for considering taking part in PROMPT!

If you would like to read more about multi-gene panels, including details about specific genes, please visit our informational website at www.promptstudy.info.

15 Argonaut, Aliso Viejo, CA 92656 Toll Free 866 262 7943 Fax 949 900 5501 ambrygen.com