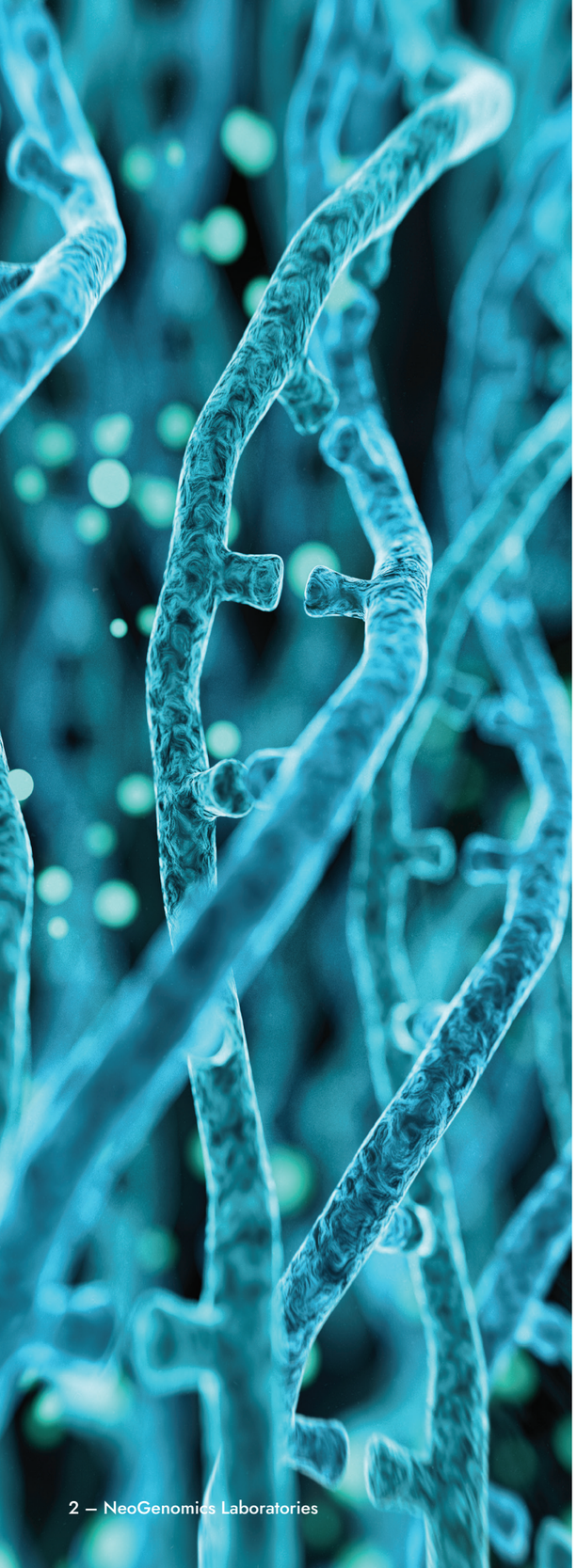
NEO GENOMICS

The **ONE LAB** you need for precision oncology breast cancer care



Biomarker use can be further optimized in breast cancer

A 2019 study assessed awareness and use of **molecular profiling in cancer treatment** from oncologists' practices[1]

Molecular profiling for breast cancer was ordered on

8%

of patients by community-based oncologists

despite high rates of clinically significant, detectable mutations.

Guideline-supported tools can inform treatment decisions in newly diagnosed or post-endocrine therapy breast cancer patients

Managing patients with early-stage breast cancer begins with knowing recurrence risk

THE PROSIGNA® BREAST CANCER PROGNOSTIC GENE SIGNATURE ASSAY

- Can assess the risk of distant recurrence within 10 years to **stratify these patients, inform prognosis, guide treatment and inform upfront patient counseling**
- Intended for use in post-menopausal women with HR+, node-negative (stage I or II), or node-positive (stage II) breast cancer who will be treated with adjuvant endocrine therapy

ASCO guidelines support its use:

- If a patient has ER/PgR-positive, HER2-negative (node-negative) breast cancer, **the clinician may use the PAM50 ROR score (Prosigna® Breast Cancer Prognostic Gene Signature Assay)**, in conjunction with other clinicopathologic variables, **to guide decisions about adjuvant systemic therapy.**[2]

Should you continue endocrine therapy if there is no recurrence after 5 years?

THE BREAST CANCER INDEX® (BCI)*

- Provides the patient's **individualized risk for distant recurrence and likelihood of benefit** from extended (>5 years) endocrine therapy
- Intended for use in women with HR+, lymph node-negative (LN-) or lymph node-positive (LN+ with 1-3 positive nodes) early-stage, invasive breast cancer who are distant recurrence-free
- If BCI is ordered at diagnosis, **0- to 10-year** results are available

ASCO guidelines support its use:

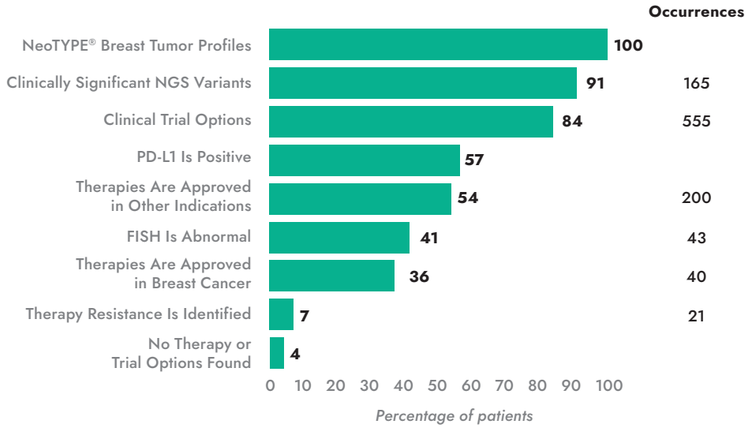
- If a patient has ER/PgR-positive, HER2-negative, node-negative breast cancer, **the clinician may use the Breast Cancer Index to guide decisions about adjuvant systemic therapy.**[2]

ASCO = American Society of Clinical Oncology.

* The Breast Cancer Index is performed, reported, and billed separately by Biotheranostics, Inc. For comprehensive details about the Breast Cancer Index, including sample reports, clinical studies, intended use and limitations, and Medicare Local Coverage Determination (LCD) criteria, visit www.breastcancerindex.com.

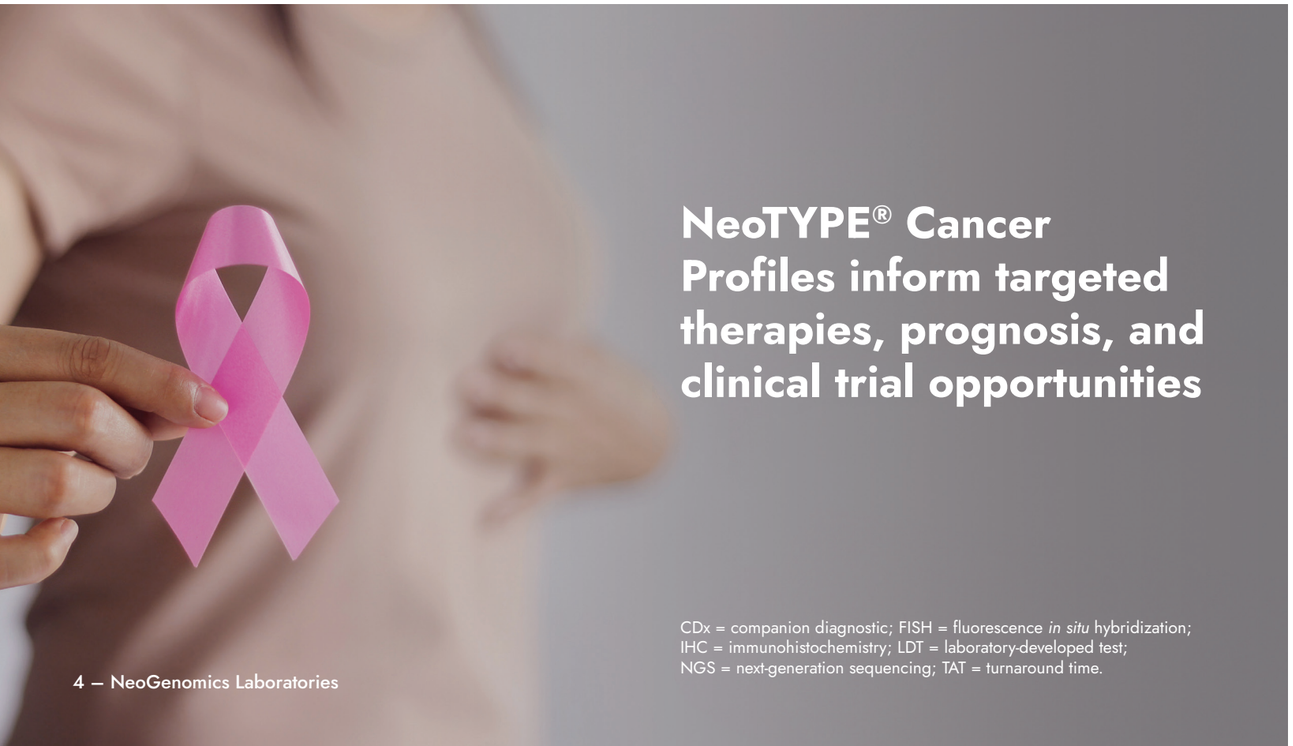
Mutation profiling: there's more to a patient's tumor than hormone status

NeoTYPE® Breast Tumor Profile can find clinically significant mutations in a patient's cancer that may impact patient management



In a recent consecutive series of 100 NeoTYPE® Breast Tumor Profile results, **96 patients had therapy implications and/or clinical trials identified**

In the series, over 500 clinical trials were identified for 84 patients. Forty therapies approved for breast cancer were identified for 36 patients, and 200 therapies approved in other indications were identified for 54 patients.



NeoTYPE® Cancer Profiles inform targeted therapies, prognosis, and clinical trial opportunities

CDx = companion diagnostic; FISH = fluorescence *in situ* hybridization; IHC = immunohistochemistry; LDT = laboratory-developed test; NGS = next-generation sequencing; TAT = turnaround time.

Biomarker testing can identify therapeutic options

NEOTYPE® BREAST TUMOR PROFILE: Mutation profiling of prognostic and predictive biomarkers for targeted therapy selection and clinical trial qualification

- Multi-method coverage of 60 biomarkers
- Immuno-oncology targets PD-L1, TMB and MSI
- Homologous recombination repair (HRR) defects
- *PIK3CA* included as LDT; separate CDx Sponsored Testing Program is available
- Pan-*TRK* detection and *NTRK*1/2/3 fusion detection

NGS: *AKT1, ARID1A, ATM, ATR, BARD1, BRAF, BRCA1, BRCA2, BRIP1, CDH1, CDK12, CHEK1, CHEK2, CTNNB1, EGFR, ESR1, ERBB2, ERBB4, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL, FGFR1, FGFR2, FGFR3, GATA3, HRAS, KIT, KRAS, MET,* Microsatellite Instability (MSI), *MLH1, MRE11A (MRE11), MSH2, MSH6, NBN, NRAS, PALB2, PIK3CA, PMS2, PTEN, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD54L, SMAD4, SMO, SRC, TERT* Promoter, *TP53,* Tumor Mutation Burden (TMB)
FISH: *MET, PTEN*
IHC: PD-L1 SP142 for TNBC, Pan-*TRK* with positive/equivocal reflex to *NTRK* 1-3 NGS fusion testing

NCCN-recommended biomarkers with FDA-approved therapies[3]

Breast Cancer Subtype	Biomarker	FDA-Approved Agents
Any	✔ *NTRK* fusion	Larotrectinib[a] Entrectinib[a]
Any	✔ MSI-H/dMMR ✔ TMB-H (≥10 muts/mb)	Pembrolizumab[b,c]
HR-positive/ HER2-negative[d]	✔ *PIK3CA* activating mutation	Alpelisib + fulvestrant[e]
HR-negative/ HER2-negative[f]	✔ PD-L1 expression • Threshold for positivity: ≥1% on tumor-infiltrating immune cells	Atezolizumab + albumin-bound paclitaxel[b]
	✔ PD-L1 expression • Threshold for positivity combined positive score ≥10	Pembrolizumab + chemotherapy (albumin-bound paclitaxel, paclitaxel, or gemcitabine and carboplatin)[b]

dMMR = deficient mismatch repair; HR = hormone receptor; IHC = immunohistochemistry; MSI-H = high microsatellite instability; mb = megabase; muts = mutations; TMB-H = high tumor mutational burden; TNBC = triple-negative breast cancer.
a Larotrectinib and entrectinib are indicated for the treatment of solid tumors that have an *NTRK* gene fusion without a known acquired resistance mutation and have no satisfactory alternative treatments or that have progressed following treatment. **b** See NCCN Guidelines® for Management of Immunotherapy-Related Toxicities. **c** Pembrolizumab is indicated for the treatment of patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, or TMB-H tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options. **d** For HR-positive/HER2-negative breast cancer, assess for *PIK3CA* mutations with tumor or liquid biopsy to identify candidates for alpelisib plus fulvestrant. *PIK3CA* mutation testing can be done on tumor tissue or ctDNA in peripheral blood (liquid biopsy). If liquid biopsy is negative, tumor tissue testing is recommended. **e** The safety of alpelisib in patients with type 1 or uncontrolled type 2 diabetes has not been established. **f** For TNBC, assess PD-L1 expression biomarker status on tumor-infiltrating immune cells to identify candidates for atezolizumab plus albumin-bound paclitaxel.
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The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available.

PIK3CA: The most common mutation in HR+/HER2- breast cancers

- **About 40% of patients with HR+ breast cancer have a *PIK3CA* mutation[5]**
- Overall, *PIK3CA* mutations are the second most common mutation observed in all breast cancer patients, second only to *TP53* mutations[4]

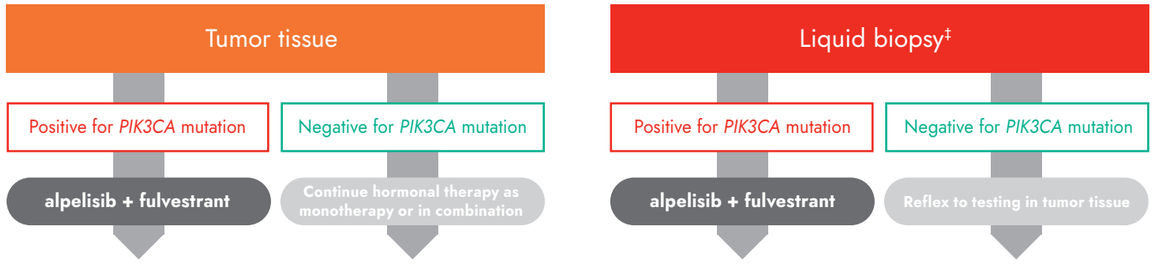
THE *PIK3CA* MUTATION TISSUE OR LIQUID BIOPSY TESTS*

are FDA-approved companion diagnostics – **available at no cost to eligible patients** – to identify HR+/HER2- patients with advanced or metastatic breast cancer (MBC) who may be **candidates for alpelisib (PIQRAY®)** therapy due to *PIK3CA* mutations.

Test for *PIK3CA* mutations when patients present with metastases from breast cancer†

Assess for *PIK3CA* mutation as part of the initial MBC workup if all of the following are true:

- ✓ **Patient has recurrent/stage IV (M1) disease**
- ✓ **Tumor is HR+/HER2-**
- ✓ **Considering therapy with alpelisib + fulvestrant†**



The *PIK3CA* Mutation CDx Testing Program provides eligible patients access to FDA-approved *PIK3CA* Mutation CDx Test by either tissue or plasma testing at no cost.*

* Part of the Novartis Sponsored Testing Program.
† Following progression on or after an endocrine-based regimen.
‡ If liquid biopsy is negative, tumor tissue testing is recommended.

Immuno-Oncology and liquid biopsy solutions for unique clinical scenarios

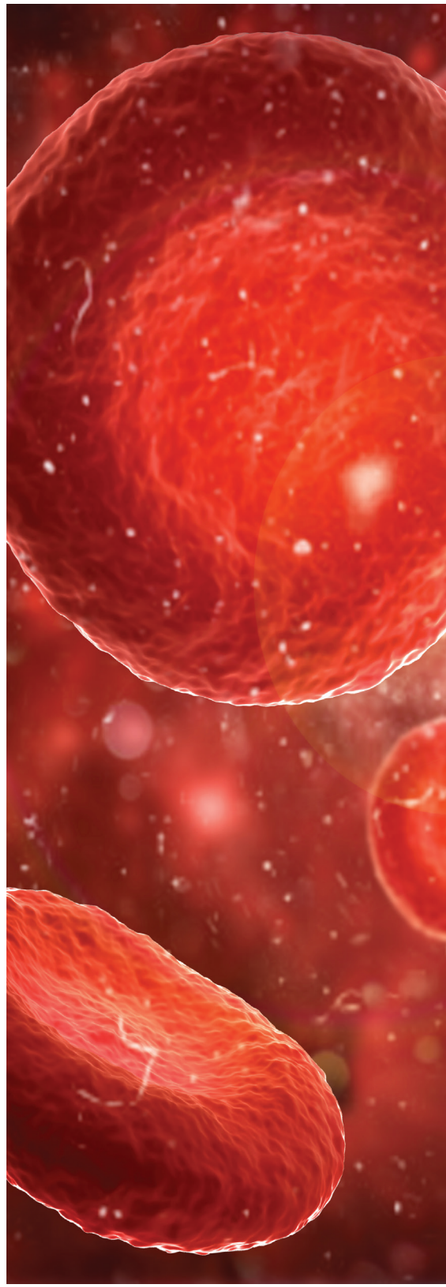
PD-L1 FOR ADVANCED TRIPLE-NEGATIVE BREAST CANCER (TNBC)

In patients with advanced, locally unresectable, or metastatic TNBC:

- The expression of the PD-L1 protein may be associated with **increased progression-free survival in patients treated with KEYTRUDA® (pembrolizumab)** and chemotherapy
  - The **PD-L1 22C3 FDA (KEYTRUDA®) IHC TEST FOR TNBC** detects PD-L1 expression in tumor cells and tumor-infiltrating immune cells, using a cut-off of ≥10 Combined Positive Score. It is an **FDA-approved companion diagnostic** for the use of KEYTRUDA® in certain TNBC cases.

LIQUID BIOPSY FOR MONITORING PROGRESSION, RESPONSE TO THERAPY OR WHEN TISSUE IS UNAVAILABLE

- **Liquid biopsy** (also called **plasma testing**) is useful when tissue is insufficient, unavailable or not practical to obtain, or when results are needed more quickly than they can be obtained from tissue analysis.
- The **NEOLAB® SOLID TUMOR LIQUID BIOPSY** is a next-generation sequencing (NGS) assay designed to detect mutations in cell-free circulating tumor DNA of patients with solid tumors (pan-cancer).
- Analytic validation demonstrated **accuracy** of 98.0%, **sensitivity** of 95.1% and **specificity** of 98.8%.



What about hereditary cancers?

TUMOR TESTING

- Tumors with the *BRCA1* and *BRCA2* mutations may respond to **PARP inhibitors** and be sensitive to **platinum-based therapy**.
- The ***BRCA1* AND *BRCA2* MUTATION ANALYSIS FOR TUMORS** test covers tumor specimen testing for these genes.
- If a tumor mutation is detected, genetic counseling and germline testing may be considered since tumor mutations may be somatic or germline.
- This is useful for limited follow-up testing when, for example, tumors had prior biomarker testing without *BRCA1* and *BRCA2*; both these genes are included in NeoTYPE® Breast, Discovery, Ovarian, and other Profiles.

The American Society of Breast Surgeons (ASBS) supports genetic testing in all patients with breast cancer:

- Recent data supports that genetic testing should be offered to **each patient with breast cancer** (newly diagnosed or with a personal history). If genetic testing is performed, such testing **should include *BRCA1/BRCA2* and *PALB2***, with other genes as appropriate for the clinical scenario and family history. For patients with newly diagnosed breast cancer, **identification of a mutation may impact local treatment recommendations** (surgery and potentially radiation) and systemic therapy.[6]

GERMLINE TESTING

- **FULGENT CANCER PANELS*** provide the opportunity to detect **pathogenic cancer susceptibility mutations**, with targeted or comprehensive testing for candidate genes, to give you information you can use now and potentially in the future.
- The ***BRCA1* AND *BRCA2* FOCUS PANEL (GERMLINE)** test covers germline testing for these genes, which suggests treatment with olaparib or talazoparib if present.
- The **FOCUS CANCER PANEL (GERMLINE)** targets 30 genes associated with a high or moderate risk for hereditary cancer syndromes where there are established clinical management guidelines for disease-causing variants.
- The **FULL COMPREHENSIVE CANCER PANEL (GERMLINE)** examines 127 genes associated with hereditary cancer, including both well-established genes and candidate genes.

The American College of Medical Genetics (ACMG) supports evaluation for genetic testing in all patients with breast cancer:

- **All patients with breast cancer** should be evaluated to **determine the need for germline genetic testing for hereditary breast cancer**. According to national practice guidelines, genetic testing for breast cancer patients is indicated based on patient characteristics, including age at diagnosis, family cancer history, expression of estrogen progesterone receptors and HER2 expression, and disease stage.[7]

PARP = poly-ADP ribose polymerase.
* Testing is performed by Fulgent Genetics.

NeoGenomics offers value

We have the depth of experience and expertise you can rely on:

620+
cancer tests available

>1 million
cancer-related tests performed per year

>4,400
hospitals, institutions and oncology offices that we work with

>100
MDs/PhDs

>435,000
patients tested per year

>19 years
serving the cancer community

13
locations across 3 continents

Results are based on 2020 volume.

NeoGenomics has you covered at all stages of breast cancer

Diagnostic · Prognostic · Predictive · Germline

Early Stage

- Breast IHC Panel and HER2 FISH
- Prosigna® Assay
- Breast Cancer Index® (BCI)
- NeoTYPE® Breast Tumor Profile
- NeoTYPE® Discovery Profile
- NeoTYPE® HRD+ Profile
- PD-L1 22C3 (KEYTRUDA®) FDA IHC for TNBC

Any Stage

- *PIK3CA* Mutation CDx – Tissue
- *PIK3CA* Mutation CDx – Plasma
- NeoLAB® Solid Tumor Liquid Biopsy
- *BRCA1* and *BRCA2* Mutation Analysis for Tumors
- Focus Cancer Panel
- Comprehensive Cancer Panel
- *BRCA1* and *BRCA2* Focus Panel

CDx = companion diagnostic; FISH = fluorescence *in situ* hybridization; HRD = homologous recombination deficiency; IHC = immunohistochemistry; TNBC = triple-negative breast cancer.

One Lab. Vital Answers.

Transforming Care for Cancer Patients.

NeoGenomics is the **One Lab** you can rely on for **vital answers** in breast cancer diagnostics throughout your patient's entire cancer experience

For more information, please contact your NeoGenomics Sales Consultant or call our Client Services Team at 866.776.5907, option 3.

References: 1. Singh BP, et al. *J Clin Oncol*. 2019;37:(suppl; abstr 10510). **2.** Andre F, et al. *J Clin Oncol*. 2019;37:1956-1964. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer. V.4.2021. ©National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed May 27, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way. **4.** Zardavas D, et al. *Breast Cancer Res*. 2014;16(1):201-210. **5.** The Cancer Genome Atlas Network. *Nature*. 2012;490(7418):61-70. **6.** American Society of Breast Surgeons. Official Statement: Consensus Guideline on Genetic Testing for Hereditary Breast Cancer. February 10, 2019. **7.** Pal T, et al. *Genet Med*. 2020;22(4):681-685.

NeoGenomics Laboratories is a specialized oncology reference laboratory providing the latest technologies, testing, partnership opportunities, and interactive education to the oncology and pathology communities. We offer the complete spectrum of diagnostic services in molecular testing, FISH, cytogenetics, flow cytometry and immunohistochemistry through our nationwide network of CAP-accredited, CLIA-certified laboratories.

NEO GENOMICS

12701 Commonwealth Dr., Suite 9
Fort Myers, FL 33913
Phone: 866.776.5907 | Fax: 239.690.4237
neogenomics.com

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