BreastTrue® High Risk Panel
Analyzing Seven Clinically Actionable Breast Cancer Genes

The Test
The BreastTrue® High Risk Panel is a seven-gene hereditary cancer panel designed for individuals and families with features suggestive of hereditary breast cancer. The seven high-risk genes included in this panel are BRCA1, BRCA2, CDH1, PALB2, PTEN, TP53, and STK11. Clinical management guidelines exist for individuals with pathogenic variants in all of these genes except PALB2, which was recently associated with a breast cancer risk of up to 58% in high-risk families.¹

Overview
Breast cancer is the most common type of cancer in women in the U.S. as well as the second leading cause of death. Overall, 1 in 8 women will develop breast cancer at some point during their lives—approximately a 12% lifetime risk of breast cancer. Although the majority of breast cancer is sporadic and caused by a combination of genetic and non-genetic factors, research has shown that approximately 5-10% of breast cancers are due to hereditary changes in single genes.²⁻³

Why Use the BreastTrue® High Risk Panel?
In a recent study describing the frequency of hereditary pathogenic variants in individuals with breast cancer, it was estimated that BRCA1 and BRCA2 account for approximately two thirds of all identified pathogenic alterations in patients with a strong personal and/or family history of breast cancer.⁴ Other highly to moderately penetrant genes accounted for the remaining third of disease-associated variants, including the five additional high-penetrance genes included on the BreastTrue® High Risk Panel.

Recently, the National Comprehensive Cancer Network (NCCN) updated their Genetic/Familial High-Risk Assessment: Breast and Ovarian practice guidelines (Version 2.2014) to review the use of multi-gene testing. Multi-gene testing allows for the simultaneous analysis of many different genes that can present with similar clinical phenotypes (as well as overlapping clinical testing criteria)—early-onset breast cancer serving as a prime example. In some families, multi-gene testing should be considered to potentially increase the detection of clinically actionable gene variants. The BreastTrue® High Risk Panel is specifically designed for families with features suggestive of hereditary breast cancer, as it analyzes seven clinically actionable genes associated with a markedly increased risk of breast cancer (see Figure 1).

When to Consider the BreastTrue® High Risk Panel
Individuals with a personal and/or family history of the following risk factors should consider the BreastTrue® High Risk Panel:

- Early onset breast cancer (diagnosed when less than 50 years old)
- Breast and ovarian cancer in the same individual
- Bilateral or multiple breast cancers in the same individual
- Triple-negative breast cancer
- Multiple relatives on the same side of the family with the same (or related) cancers
- Male breast cancer and/or other rare associated cancers (see Figure 2)
- Ashkenazi Jewish ancestry
- Other cancers associated with hereditary breast cancer genes (see Figure 2)
Breast Cancer Risks
The lifetime female breast cancer risk for each of the genes included in the BreastTrue® High Risk Panel is shown below:

Other Associated Cancer Risks
In addition to breast cancer, pathogenic variants in each of the genes in the BreastTrue® High Risk Panel are associated with increased risks for other cancers. Being aware of these additional cancer risks is important for effective screening for each individual patient. Other cancers associated with each gene in the panel are shown in Figure 2.

**Figure 2:** Cancer types associated with pathological variants in each of the respective genes on the BreastTrue® High Risk Panel. In the figure above, ◆ represents a well-defined increased cancer risk, while * represents a potential increased cancer risk that has not yet been well defined. Please note that additional cancers may also be associated with pathological alterations in these genes, but that are not represented in this figure.
Test Specifications
The BreastTrue® High Risk Panel uses next-generation sequencing technology with Sanger confirmation of all gene variants. The average read depth of the test is 5,000x/bp, and coverage includes 20 bp into all intron/exon borders. Sanger fill-in is used for all genes in areas of low coverage, which is defined as a read depth of less than 25x. Additionally, a custom array CGH assay is used to detect large deletions and duplications in all seven genes. This combination of methodologies results in an overall test sensitivity of >99.99%, with a test specificity of 99.97%.

References