**Integrated BRACAnalysis® with Myriad myRisk™ Hereditary Cancer**

### myRisk Genetic Result

**RESULT: POSITIVE - CLINICALLY SIGNIFICANT MUTATION IDENTIFIED**

Note: "CLINICALLY SIGNIFICANT," as defined in this report, is a genetic change that is associated with the potential to alter medical intervention.

<table>
<thead>
<tr>
<th>GENE</th>
<th>MUTATION</th>
<th>INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BARD1</strong></td>
<td>c.xxxx (p.xxxx*)</td>
<td>Elevated Cancer Risk</td>
</tr>
<tr>
<td></td>
<td>Heterozygous</td>
<td></td>
</tr>
</tbody>
</table>

**Details About: BARD1 c.xxxx (p.xxxx*): NM_000465.3**

**Functional Significance: Deleterious - Abnormal Protein Production and/or Function**

The heterozygous germline BARD1 mutation c.xxxx is predicted to result in the premature truncation of the BARD1 protein at amino acid position xxx (p.xxxx*).

**Clinical Significance: Elevated Cancer Risk**

This mutation is associated with increased cancer risk and should be regarded as clinically significant.

**ADDITIONAL FINDINGS: NO VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED**

**Details About Non-Clinically Significant Variants:** All individuals carry DNA changes (i.e., variants), and most variants do not increase an individual's risk of cancer or other diseases. When identified, variants of uncertain significance (VUS) are reported. Likely benign variants (Favor Polymorphisms) and benign variants (Polymorphisms) are not reported and available data indicate that these variants most likely do not cause increased cancer risk. Present evidence does not suggest that non-clinically significant variant findings be used to modify patient medical management beyond what is indicated by the personal and family history and any other clinically significant findings.

**Variant Classification:** Myriad's myVision™ Variant Classification Program performs ongoing evaluations of variant classifications. In certain cases, healthcare providers may be contacted for more clinical information or to arrange family testing to aid in variant classification. When new evidence about a variant is identified and determined to result in clinical significance and management change, that information will automatically be made available to the healthcare provider through an amended report.

### ADDITIONAL INFORMATION

**GENES ANALYZED**

Unless otherwise noted sequencing and large rearrangement analyses were performed on the following genes:

- APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM (large rearrangement only), MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53.

**Indication for Testing:** It is our understanding that this individual was identified for testing due to a personal or family history suggestive of a hereditary predisposition for cancer.

**Associated Cancer Risks and Clinical Management:** Please see the "myRisk Management Tool" associated with this report for a summary of cancer risk and professional society medical management guidelines that may be useful in developing a plan for this patient based on test results and reported personal/family history, if applicable. Testing of other family members may assist in the interpretation of this patient's test result.

**Analysis Description:** The Technical Specifications summary (MyriadPro.com/myRisk) describes the analysis, method, performance, nomenclature, and interpretive criteria of this test. The classification and interpretation of all variants identified in this assay reflects the current state of scientific understanding at the time this report was issued, and may change as new scientific information becomes available. The interpretation of this test may be impacted if the patient has a hematologic malignancy or an allogeneic bone marrow transplant.
myRisk Genetic Result

Name: Pt Last Name, Pt First Name
DOB: 
Accession #: 07003814-BLD
Report Date: Jul 23, 2014

Please contact Myriad Medical Services at 1-800-469-7423 X 3850 to discuss any questions regarding this result.

This Authorized Signature pertains to this laboratory report:

Benjamin B. Roa, PhD
Diplomate ABMG
Laboratory Director
Richard J. Wenstrup, MD
Diplomate ABMG
Chief Medical Officer

These test results should only be used in conjunction with the patient's clinical history and any previous analysis of appropriate family members. The patient's clinical history and test results should not be disclosed to a third party, unless related to treatment or payment for treatment, without the patient's express written authorization. It is strongly recommended that these results be communicated to the patient in a setting that includes appropriate counseling. This test was developed and its performance characteristics determined by Myriad Genetic Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that clearance or approval for laboratory-developed tests is not required.
**result:** positive - clinically significant mutation identified

Note: "clinically significant," as defined in this report, is a genetic change that is associated with the potential to alter medical intervention.

**Additional Findings:** no variant(s) of uncertain significance (vus) identified

<table>
<thead>
<tr>
<th>Gene</th>
<th>Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>BARD1</td>
<td>c.xxxx (p.xxxx*)</td>
</tr>
</tbody>
</table>

This genetic test result is associated with the following cancer risks:

**Elevated Risk:** Female Breast

**Personal/Family History Summary and Management Information**

<table>
<thead>
<tr>
<th>Family Member</th>
<th>Cancer / Clinical Diagnosis</th>
<th>Age at Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Aunt Maternal</td>
<td>Breast, Invasive</td>
<td>45</td>
</tr>
<tr>
<td>Uncle Maternal</td>
<td>Colorectal</td>
<td>55</td>
</tr>
</tbody>
</table>

This information was provided by a qualified healthcare provider on the test request form and was not verified by Myriad. Family members listed as "other" are not included in personal/family history assessment.

Beyond the genetic result, no modified management guidelines identified; other clinical factors may influence individualized management.
OVERVIEW

BARD1-associated Cancer Risk:

• This patient has been found to have a mutation in the BARD1 gene. BARD1 mutations have been found in families suspected of having a form of Hereditary Breast and Ovarian Cancer syndrome (HBOC), but without detectable mutations in BRCA1 or BRCA2, with almost all of the mutations found in patients with breast cancer. Therefore, it is believed that women with BARD1 mutations have an increased risk for breast cancer. There is not sufficient evidence at this time to say that there is also an increased risk for ovarian cancer in women with BARD1 mutations.

• At this time, there are no known cancer risks for men due to mutations BARD1.

• There are currently no widely accepted guidelines for the medical management of women with BARD1 mutations, and the exact breast cancer risk is not known. Medical management options based on other conditions which increase the risk of breast cancer are listed below. Since information about the cancer risks associated with BARD1 mutations is relatively new, and there is uncertainty about the best ways to reduce these risks, it may be appropriate to interpret these results in consultation with cancer genetics professionals who have expertise in this emerging area of knowledge.

WHAT ARE THE PATIENT'S GENE-RELATED CANCER RISKS?

If more than one gene mutation increases a specific cancer risk (e.g., breast), only the highest cancer risk is shown. If this patient has more than one gene mutation, risks may be different, as this analysis does not account for possible interactions between gene mutations.

<table>
<thead>
<tr>
<th>CANCER TYPE</th>
<th>CANCER RISK</th>
<th>RISK FOR GENERAL POPULATION</th>
<th>RELATED TO</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEMALE BREAST</td>
<td>Elevated risk</td>
<td>10.2%</td>
<td>BARD1</td>
</tr>
</tbody>
</table>

WHAT MANAGEMENT FOR CANCER RISKS SHOULD BE CONSIDERED?

This overview of clinical management guidelines is based on this patient's personal and family history and genetic test results. Unless otherwise stated, medical management guidelines are limited to those issued by the National Comprehensive Cancer Network (NCCN). The reference provided should always be consulted for more details. If management for a specific cancer (e.g. breast) is available due to multiple causes (e.g. a mutation and a family history, or multiple mutations in different genes), only the most aggressive management is shown. Only guidelines for the patient's long-term care related to cancer prevention are included.

No information is provided related to treatment of a previous or existing cancer or polyps. These recommendations may require modification based on the patient's personal medical history, surgeries and other treatments. Patients with a personal history of cancer, benign tumors or pre-cancerous findings may be candidates for long term surveillance and risk reduction strategies beyond what is necessary for the treatment of their initial diagnosis. Any discussion of medical management options is for general information purposes only and does not constitute a recommendation. While genetic testing and medical society guidelines provide important and useful information, medical management decisions should be made in consultation between each patient and his or her healthcare provider.
Currently there are no specific medical management guidelines for breast cancer risk in mutation carriers. However, the possibility of an increased risk for breast cancer warrants consideration of individualized breast cancer risk reduction strategies, as well as the modification of standard population screening recommendations by starting screening at younger ages and/or performing screenings at greater frequency.¹,²


Notes for Personalized Management:

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**myRisk Management Tool**

**Name:** Pt Last Name, Pt First Name  
**DOB:**  
**Accession #:** 07003814-BLD  
**Report Date:** Jul 23, 2014

- The Genetic Test Result Summary includes: female breast, male breast, colorectal, endometrial, gastric, ovarian, pancreatic and prostate cancers, and melanoma. In this summary a gene associated cancer risk is described as "High Risk" for a cancer type if all of the following conditions are met: the absolute risk of cancer is approximately 5% or higher, the increase in risk over the general population is approximately 3-fold or higher, and there is significant data from multiple studies supporting the cancer risk estimate. A gene is described as "Elevated Risk" for a cancer type if there is sufficient data to support an increase in cancer risk over the general population risk, but not all criteria for "High Risk" are met.

**INFORMATION FOR FAMILY MEMBERS**

Family members should talk to their healthcare providers about hereditary cancer testing to help define their own risk and assist in the interpretation of this patient's genetic test result.

- This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

- **Family members should talk to a healthcare provider about genetic testing.** Close relatives such as parents, children, brothers, and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance for carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention. More resources for family testing are available at MySupport360.com.

- At this time, there are no known cancer risks for men due to mutations in BARD1. Therefore, there are no entries for male relatives in the cancer risk table below.

**CANCER RISK FOR BARD1 CLINICALLY ACTIONABLE MUTATION**

<table>
<thead>
<tr>
<th>CANCER TYPE</th>
<th>CANCER RISK</th>
<th>RISK FOR GENERAL POPULATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOR FEMALE RELATIVES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEMALE BREAST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>To age 80</td>
<td>Elevated risk</td>
<td>10.2%</td>
</tr>
</tbody>
</table>

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END OF MYRISK MANAGEMENT TOOL