**Assay Description:** The Prosigna® breast cancer gene signature assay measures the expression of 50 different genes to identify subtype and report a Risk of Recurrence Score (ROR), which is used to assign the patient to a predefined risk group. These results are derived from a proprietary algorithm based on the PAM50 gene signature, intrinsic subtype, and clinical variables including tumor size and nodal status.

**Probability of Distant Recurrence:**
In the clinical validation studies, patients who were node-negative, luminal B subtype, with an ROR score of 70 were in the high-risk group. This group averaged a 22% probability of distant recurrence at 10 years.

The Prosigna® algorithm has been validated by 2 randomized clinical trials including more than 2400 patients with varying rates of distant recurrence. An analysis of these 2 clinical validation studies shows that the probability of distant recurrence for the high-risk population is 22%.†

<table>
<thead>
<tr>
<th>Low risk</th>
<th>Intermediate risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group average: 4%</td>
<td>Group average: 11%</td>
<td>Group average: 22%</td>
</tr>
<tr>
<td>95% CI: 3%-5%</td>
<td>95% CI: 8%-14%</td>
<td>95% CI: 18%-27%</td>
</tr>
</tbody>
</table>

For more information, visit PROSIGNA.com or e-mail info@prosigna.com

†Data apply to patients being treated with hormone therapy for 5 years as in the tested patient population. See Package Insert for further information on therapy regimens and tested patient population. It is unknown whether these findings can be extended to other patient populations or treatment schedules.
Patient Specimen Run Set ID: Prosigna Sample 2
ID #: n0-I2-70-HR-LB
Date Reported: September 20, 2017

Run Set ID: Prosigna Sample 2
ID #: n0-I2-70-HR-LB
Date Reported: September 20, 2017

Specimen
Tumor Size: <= 2cm
Lymph Nodes: node-negative

Clinical Validation Studies: Prognosis for node-negative, luminal B, high-risk breast cancer patients was determined based on the rate of distant recurrence (DR) of this population in 2 prospective-retrospective clinical studies. These studies analyzed more than 2400 samples from postmenopausal women with early stage, hormone receptor-positive breast cancer, using a prospectively defined analysis plan. The data shown are for postmenopausal women with early stage, hormone receptor-positive breast cancer who received 5 years of endocrine therapy after surgical resection of the primary tumor.

Rate of Distant Recurrence (DR) for Node-Negative Patients

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Rate of DR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal A</td>
<td>5%</td>
<td>[4%-7%]</td>
</tr>
<tr>
<td>Luminal B</td>
<td>18%</td>
<td>[15%-22%]</td>
</tr>
<tr>
<td>HER2-enriched</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Basal-like</td>
<td>*</td>
<td></td>
</tr>
</tbody>
</table>

*There were insufficient numbers of basal-like and HER2-enriched patients in these studies to produce data.

Subtype and Prognosis:
Intrinsic subtype is related to prognosis in the tested patient population. The most common subtypes of breast cancer are the luminal subtypes: luminal A and luminal B. In the combined analysis of 2 clinical validation studies of hormone receptor-positive patients, 68% of the tested patient population was found to be luminal A, and 27% was luminal B. The gene expression pattern of these subtypes resembles the luminal epithelial component of the breast. These tumors are characterized by high expression of estrogen receptor (ER), progesterone receptor (PR), and genes associated with ER activation. Luminal A breast cancers exhibit low expression of genes associated with cell cycle activation and generally have a better prognosis than luminal B.

The TransATAC study analyzed 1007 samples using a prospectively defined analysis plan. Data shown are for postmenopausal stage I or II, node-negative, hormone receptor-positive breast cancer patients that received 5 years of endocrine therapy.*

The ABCSG-8 study analyzed 1478 samples using a prospectively defined analysis plan. Data shown are for postmenopausal stage I or II, node-negative, hormone receptor-positive breast cancer patients that received 5 years of endocrine therapy.*

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*See Package Insert for further information on therapy regimens and tested patient population. It is unknown whether these findings can be extended to other patient populations or treatment schedules.

REFERENCES: