Researchers Identify Splice Variant of Breast Cancer Gene that Can Mask Risk of Recurrence

'High Risk' Patients with Unusual Hormone Receptors May Be Undertreated

IRVINE, CA and AMSTERDAM, THE NETHERLANDS, August 27, 2013 – Agendia, a leader in molecular cancer diagnostics, announced today that researchers have identified a subset of breast cancer patients whose standard biomarker tests may incorrectly classify patients as "low risk" and benefitting from endocrine therapy. A study published this month in *Breast Cancer Research and Treatment** concluded that this subset of breast cancer patients may actually be at "high risk" of disease progression and benefit more from chemotherapy than endocrine therapy.

The researchers found that 2 percent of breast cancer patients tested, who were identified as estrogen receptor positive (ER+) and therefore potential candidates to benefit from endocrine therapy, actually had a variant of the estrogen receptor called "delta Exon 7 deletion." This variant is missed by standard receptor testing and reported as receptor positive, when in fact the variant protein inhibits the normal estrogen signal in the cell that may prevent the patient from benefitting from routine endocrine therapy. Moreover, these patients have a genomic profile of their tumor that suggests that 95% of these are "at high recurrence risk and would likely benefit from adjuvant chemotherapy," the researchers concluded.

The researchers identified the importance of the delta Exon 7 deletion through a test called BluePrint®, which was developed by Agendia. BluePrint is one part of a suite of related breast cancer tests called Symphony, which provides a complete view of a patient's prognosis and helps guide their individual treatment decisions through genomic profiling.

"The researchers identified the presence of the Exon 7 variant of the estrogen receptor while trying to determine why some breast cancer patients who tested ER+ in the classical test for receptor status turned out to be of the 'basal-like' subtype by the BluePrint assay, which indicates a lack of a functional estrogen pathway," noted Stephanie R. Akbari, M.D., Medical Director of the Reinsch Pierce Family Center for Breast Health at Virginia Hospital Center, a member of the research team. "Medical experts have long established that ER+ tumors typically benefit from hormonal therapies, but we also know that not all patients with ER+ tumors benefit from this therapy. This finding may help identify those patients that are unlikely to benefit from hormonal therapy."

Dr. Akbari said, "Our findings show that, as we discover the importance of splicing variants such as Exon7, additional molecular subtyping of a patient's tumor is necessary to reach a more accurate understanding of the disease."

Agendia CEO David Macdonald said, "Agendia's Symphony is the only commercially available test suite that provides molecular subtyping and can identify the growing body of important genetic variants such as Exon 7. This research underscores Agendia's commitment to ongoing discovery and collaboration between industry and physician-directed research in bringing scientific advances into clinical practice."

About Agendia:
Agendia is a leading molecular diagnostic company that develops and markets FFPE-based genomic diagnostic products. Agendia's breast cancer Symphony™ suite was developed by analyzing the complete human genome, ensuring 100% definitive results for cancer patients. Together, these tests help physicians determine a patient's

individual risk for metastasis, which patients will benefit from chemo, hormonal, or combination therapy, and which patients do not require these treatments and can instead be treated with other less arduous and less costly methods. MammaPrint®, the initial test in the Symphony suite is the only FDA cleared test which determines recurrence risk in breast cancer patients.

In addition to the Symphony suite of tests, Agendia has a rich pipeline of genomic products in development. The Company collaborates with pharmaceutical companies, leading cancer centers and academic groups to develop companion diagnostic tests in the area of oncology and is a critical partner in the ISPY-2 and MINDACT trials. For more information, please visit www.agendia.com.

*Breast Cancer Res. Treat. 140:475–484 (2013).

For further information, please contact:

Allen & Caron Inc.
Matt Clawson or
Len Hall (Financial Media)
949-474-4300
matt@allencaron.com
len@allencaron.com