Bionano Announces First Study Using OGM to Discover Structural Variants with Potential Relevance to Genetic Diagnosis of MRKH Syndrome, a Syndrome Impacting Reproductive System Development in 1 in 4,500 Females

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- Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome is among several forms of Müllerian agenesis, a disorder impacting 1 in 4,500 females which is indicated by the absence or underdevelopment of the female reproductive system
- Researchers in the study hypothesized that a genome-wide structural variant (SV) analysis would result in the identification of rare SVs relevant to MRKH's genetic etiology, which might lead to better understanding of the syndrome and ultimately inform potential therapies and treatment
- OGM was used to analyze samples from 47 parents and 87 individuals with MRKH, to detect a variety of rare SVs that may be linked to MRKH

SAN DIEGO, March 22, 2023 (GLOBE NEWSWIRE) -- Bionano Genomics, Inc. (Nasdaq: BNGO) today announced the publication of the first study to evaluate optical genome mapping (OGM) as a method to identify rare structural variants (SVs) that might contribute to the development of Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome. MRKH is one of several forms of Müllerian agenesis, a disorder that affects 1 in 4,500 females and impacts patients' reproductive systems and potential ability to carry a pregnancy. Molecular diagnosis is helpful in determining the best treatment for MRKH, but because genetic causes are largely unknown, research into this prevalent class of disorders is key to enabling effective therapies. In this study, researchers used OGM to analyze MRKH samples to detect a variety of SVs that may be relevant to MRKH's genetic etiology in a single assay.

MRKH is a syndrome that impacts approximately 7-10% of females and presents with two distinct clinical phenotypes that primarily affect the female reproductive system:

- The condition causes the vagina and uterus to be underdeveloped or absent, and affected patients are usually unable to carry a pregnancy
- MRKH is often identified at puberty when a female does not begin menstruating
- Type I consists of congenital absence/hypoplasia of reproductive organs
- Type II may also be associated with skeletal, auditory, and/or cardiac valve abnormalities

The research study from Augusta University used OGM to analyze samples from 87 individuals with MRKH.

- MRKH was defined as the congenital absence of the uterus and vagina with or without associated anomalies
- Samples from 47 parents were also analyzed since there is evidence for a genetic component in some patients based upon the presence of more than one affected individual in a family
- Findings were confirmed with quantitative PCR or SNP arrays to confirm larger deletions; additional confirmation was done with karyotype (KT) and fluorescent in situ hybridization (FISH)

The study authors selected OGM to analyze MRKH samples, citing its resolution and sensitivity when compared to traditional cytogenetic methods.

- Because of the elusiveness of identifying genes involved in MRKH, and because large structural and copy number variants (CNVs) have been associated with MRKH, the study authors hypothesized that a high-resolution genome-wide SV analysis would result in the identification of potentially relevant rare SVs in individuals with MRKH
- The study authors stated that current cytogenetic methods used for MRKH analysis have limitations, including karyotyping (KT) which has low resolution and chromosomal microarray (CMA) which has low sensitivity for low-level mosaicism, thought to play a role in the cause of the syndrome
- Additionally, DNA sequencing has not been successful except for those cases with WNT4 or HNF1B pathogenic variants
- The study authors commented that OGM is a sensitive molecular method that has the capability to detect a variety of different types of SVs in the same assay

Using OGM, researchers were able to identify rare SVs that could potentially help explain the genetic basis of the syndrome:

- 14 structural variants (SVs) with potential involvement in MRKH, including seven deletions, three duplications, two translocations, and two aneuploidies, were detected in 19.5% of probands [17 out of 87] and confirmed with orthogonal methods
- 19 additional SVs with potential relevance to MRKH were detected in 27.6% of probands [24 out of 87]
- Mosaicism was detected in 21.4% of confirmed variants [3 out of 14]
- Researchers identified the first described female with MRKH to possess mosaicism for trisomy 12, which potentially confirms a genetic driver that researchers have thought to be linked to MRKH

"We are pleased to see the first study to use OGM to investigate possible genetic causes of MRKH, which is a rare disease which impacts female

fertility and that has long challenged the research community. The study, led by Dr. Lawrence Layman, concluded that OGM detected SVs in known and candidate genes associated with MRKH with high resolution and sensitivity for multiple variant classes in a single assay and this may improve our understanding of the cause of the disease. We believe the authors' findings that indicate mosaicism, including for a trisomy 12, could be involved in the pathogenesis of MRKH were particularly significant," commented Erik Holmlin, PhD, president and chief executive officer of Bionano.

This publication can be found here.

About Bionano Genomics

Bionano Genomics is a provider of genome analysis solutions that can enable researchers and clinicians to reveal answers to challenging questions in biology and medicine. The Company's mission is to transform the way the world sees the genome through OGM solutions, diagnostic services and software. The Company offers OGM solutions for applications across basic, translational and clinical research. Through its Lineagen, Inc. d/b/a Bionano Laboratories business, the Company also provides diagnostic testing for patients with clinical presentations consistent with autism spectrum disorder and other neurodevelopmental disabilities. Through its BioDiscovery business, the Company also offers an industry-leading, platform-agnostic software solution, which integrates next-generation sequencing and microarray data designed to provide analysis, visualization, interpretation and reporting of copy number variants, single-nucleotide variants and absence of heterozygosity across the genome in one consolidated view. For more information, visit www.bionanogenomics.com, www.bionanolaboratories.com or www.biodiscovery.com

Bionano's OGM products are for research use only and not for use in diagnostic procedures.

Forward-Looking Statements of Bionano Genomics

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "believe," "could," "should," "potential," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) convey uncertainty of future events or outcomes and are intended to identify these forward-looking statements. Forward-looking statements include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, OGM's utility for genetic disease research including for Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome, OGM's ability to detect SVs relevant to the MRKH syndrome, and the ability and utility of OGM to detect SVs compared to traditional cytogenetic methods. Each of these forward-looking statements involves risks and uncertainties. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. Factors that may cause such a difference include the risks and uncertainties associated with: global and macroeconomic events, such as the impact of the COVID-19 pandemic and the ongoing Ukraine-Russian conflict and related sanctions, on our business and the global economy; general market conditions; changes in the competitive landscape and the introduction of competitive technologies or improvements to existing technologies; failure of OGM to prove useful for research in areas including rare genetic diseases, including the MRKH syndrome; the ability of OGM better detect SVs when compared to traditional cytogenetic methods; future study results contradicting the results reported in the paper referenced in this press release; changes in our strategic and commercial plans; our ability to obtain sufficient financing to fund our strategic plans and commercialization efforts; the ability of medical and research institutions to obtain funding to support adoption or continued use of our technologies; and the risks and uncertainties associated with our business and financial condition in general, including the risks and uncertainties described in our filings with the Securities and Exchange Commission, including, without limitation, our Annual Report on Form 10-K for the year ended December 31, 2022 and in other filings subsequently made by us with the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made and are based on management's assumptions and estimates as of such date. We do not undertake any obligation to publicly update any forward-looking statements, whether as a result of the receipt of new information, the occurrence of future events or otherwise.

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