Results Presented at AGBT Demonstrate Clinical Significance of Next-Generation Mapping to Improve Serious Human Disease Research and Potentially Patient Outcomes

SAN DIEGO, CA – February 15, 2017 – Bionano Genomics, a company focused on genome structure analysis, today highlighted study results that demonstrate the translational and clinical significance of next-generation mapping (NGM) to improve serious human disease research by precisely detecting large structural variations (SVs) often missed by other technologies such as sequencing. Research is being presented at the Advances in Genome Biology and Technology (AGBT) General Meeting this week.

Erik Holmlin, Ph.D., CEO of Bionano, commented, "Large genomic rearrangements are increasingly understood as drivers of serious human health conditions. Sequencing solutions based on short reads do not capture these SVs with sufficient sensitivity and specificity to enable comprehensive studies of their biological and clinical significance and even long read sequencing does not overcome these limitations. Results of these four studies demonstrate the ability of Bionano's next-generation mapping to accurately detect large SVs, many of which have critical clinical implications with the potential to meaningfully improve patient outcomes. We look forward to sharing these results with researchers at AGBT this week."

Key findings from four of the studies being presented include:

Poster #814: Detecting a novel range of large somatic genomic rearrangements in human cancer using the Bionano Optical mapper

Vanessa Hayes, Ph.D., Lab Head of Human Comparative and Prostate Cancer Genomics, Garvan Institute of Medical Research, and her team demonstrate NGM as a complimentary tool to next-generation sequencing (NGS) due to NGM's ability to examine megabase length DNA molecules outside the detection range of NGS. Using optical mapping with Bionano's Irys® System, the researchers generated complete human genome maps from tumor-normal pairs of both primary and metastatic prostate cancer from five prostate cancer patients, and identified a novel set of large SVs within prostate cancer, of which almost 90% were undetectable using NGS alone. Use of NGS and NGM methods allowed for verification of up to 95% of the large SVs identified through NGM. Most importantly, the researchers identified a target mutation of drug metabolism in the NGM results that was completely missed by NGS. This finding could have guided patient treatment, illustrating the significant need to accurately and comprehensively detect large SVs that have clinical implications in serious human health conditions, including cancer.

Poster #516: Potential for improved molecular diagnosis of FSHD through D4Z4 array quantitation using Bionano technology

Jonathan Pevsner, Ph.D., Professor at the Kennedy Krieger Institute and Johns Hopkins University School of Medicine, and his team used NGM with Saphyr to determine the genomic architecture of specific regions of chromosomes associated with Facioscapulohumeral muscular dystrophy (FSHD), one of the most common hereditary form of muscle disease for which genetic testing, while sensitive and specific, is also complex, laborious, and specialized. 95% cases of FSHD have a defect in FSHD1 gene that is associated with contraction of a 3.3 kilobase D4Z4 repeat in the subtelomeric region of chromosome 4q35. The researchers assembled D4Z4 genome maps from normal individuals and FSHD patients, and demonstrated

that NGM correctly distinguished between the pathogenic and the non-pathogenic allele, correctly determined the number of D4Z4 repeats on chromosome 4 while at the same time distinguishing it from the non-relevant but highly similar repeat on chromosome 10. Whole-genome sequencing and 10X-Genomics sequencing failed to resolve this locus or to distinguish the chromosome 4 and 10 repeats.

Poster #1009: Structural variation landscape across 26 human populations reveals population specific variation patterns in complex genomic regions

Han Cao, Ph.D., Founder and Chief Scientific Officer at Bionano Genomics, presents the results of collaborators at the University of California, San Francisco (UCSF), Drexel University, and Chinese University of Hong Kong. The team examined the sensitivity of detection and localization of SVs in human populations. Researchers constructed genome optical maps using Irys for 146 unrelated individuals from 26 human populations with long DNA molecules (>150 kb) using native DNA without amplification and then *de novo* assembled the map without the use of the NGS-generated human reference genome assembly. The NGM-generated optical maps showed clear specific SV patterns among different ethnic groups and individuals in the population, with patterns most pronounced in complex regions of the genome where large (>50 kb) inversions and tandem duplications are mixed together in the same loci. The study demonstrates the power of long single-molecule NGM in resolving complex SVs in the human genome beyond the ability of NGS. Furthermore, it explains the need to create specific reference genomes for a wide range of ethnically diverse populations to allow for precision medicine initiatives reflecting the correct genomic structure of each patient.

Poster #1116: Efficient de novo structural variation analysis and annotation using next-generation mapping (NGM) with the Bionano Irys System

Andy Wing Chun Pang, Ph.D., Senior Scientist at Bionano Genomics, and the Bionano team demonstrate the significance of NGM using Irys to discover *de novo* SV mutations that are associated with genetic disease and can be missed by NGS and microarray. Blood samples were obtained from a quintet family with all three children displaying developmental delay, and for each individual, DNA molecules larger than 150 kbp were extracted and assembled *de novo*, creating megabases-long optical maps. The process from sample collection to SV-discovery took only one week. In each sample, researchers detected more than 3,500 insertions and deletions of lengths more than 500 bp, and discovered five to seven *de novo* SVs in the affected children, one of which was shared among all three and possibly associated with developmental delay. The study suggests that Irys may replace conventional approaches for rapid discovery of functionally-relevant variants, and overall, significantly improves deeper understanding of genomes.

Learn more by visiting **Bionano's Saphyr Room # 213** at AGBT and visiting www.bionanogenomics.com/AGBT2017.

About Bionano Genomics®

Bionano Genomics, Inc. provides the Irys and Saphyr systems for next-generation mapping (NGM), which is the leading solution in physical genome mapping. NGM offers customers whole genome analysis tools that reveal true genome structure and enabling researchers to capture what's missing in their data to advance human, plant and animal genomic research. NGM uses NanoChannel arrays to image DNA at the single-molecule level with average single-molecule lengths of about 350,000 base pairs, which leads the genomics industry. The long-range genomic information obtained with NGM detects and deciphers structural variations (SVs), which are large, complex DNA segments involving repeats that are often missed by sequencing technologies and which are a leading cause of inaccurate and incomplete genome

assembly.

As a stand-alone tool, NGM enables the accurate detection of SVs, many of which have been shown to be associated with human disease as well as complex traits in plants and animals. As a complementary tool to next-generation sequencing (NGS), NGM integrates with sequence assemblies to create contiguous hybrid scaffolds for reference-quality genome assemblies that reveal the highly informative native structure of the chromosome. NGM also provides the additional ability to verify, correct and improve a NGS-generated genome assembly.

Only Bionano provides long-range genomic information with the cost-efficiency and high throughput to keep up with advances in NGS.

NGM has been adopted by a growing number of leading institutions around the world, including: National Cancer Institute (NCI), National Institutes of Health (NIH), Wellcome Trust Sanger Institute, BGI, Garvan Institute, Salk Institute, Mount Sinai and Washington University. Investors in the Company include Domain Associates, Legend Capital, Novartis Venture Fund and Monashee Investment Management.

For more information, please visit www.BionanoGenomics.com.

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