Nature Genetics Paper Demonstrates How Inclusion of Bionano Genomics' Next-Generation Mapping is Essential to Create the Most Complete and Accurate *De Novo* Mammalian Genome Assembly

SAN DIEGO, CA – March 9, 2017 – Bionano Genomics®, Inc., a company focused on genome structure analysis, today highlighted results from a study demonstrating how combining genomic sequencing and mapping technologies, including Bionano's next-generation mapping (NGM), produced the most continuous *de novo* mammalian assembly to date, of the domestic goat (*Capra hircus*). The paper, "Single-molecule sequencing and chromatin conformation capture enable de novo reference assembly of the domestic goat genome," was published online in advance of print in the March 6, 2017 issue of *Nature Genetics* (DOI:10.1038/ng.3802).

The paper described the use of single-molecule real-time long-read sequencing for contig formation (PacBio's RSII), followed by scaffolding using chromatin interaction mapping (Phase Genomics' Hi-C) and optical mapping data (Bionano Genomics' Irys®). The resulting assembly was polished with paired-end short-read sequencing for sequence accuracy (Illumina's HiSeq).

Hi-C has been gaining popularity for scaffolding *de novo* assembled genomes. By cross-linking remote regions of chromosomes, Hi-C has the potential to make scaffolds reaching chromosome arm lengths possible. However, this cross-linking does not always enable order and orientation of the contigs to be determined correctly. In the scaffolding of the goat genome described here, Hi-C introduced 7 times more errors than Bionano (21 vs. 3).

Since Bionano NGM is the only non-sequence based scaffolding method, it is the only technology capable of correcting errors inherent to both short-read and long-read sequencing. Bionano genome maps are created completely *de novo*, and therefore provide an entirely independent assembly with which to compare the sequence contigs. The *Nature Genetics* paper describes how Bionano's genome maps were able to correct 36 mis-assemblies in the PacBio contigs. Furthermore, Bionano allowed for precise sizing of 79% of the remaining gaps, which is not possible with Hi-C.

Erik Holmlin, Ph.D., CEO of Bionano, commented, "This paper follows the recent release of multiple reference-quality human genomes, including the Chinese and Korean reference genomes, all of which included Bionano data to create the most contiguous and accurate assemblies possible. Since the time this study was conducted over 18 months ago, Bionano has significantly advanced its scaffolding tools and with the recently released Saphyr™ instrument, the cost to map a mammalian genome has decreased six-fold. This publication serves as important validation of NGM as a complementary genomic tool to combine with next-generation sequencing to reveal highly informative native structure of chromosomes."

Bionano's hybrid scaffold pipeline within the Bionano Access™ analysis and visualization software allows users to combine two genome maps, each created by labeling a different sequence motif with an NGS assembly. This combination typically doubles the contiguity achieved using one genome map, incorporates about 50% more contigs into the assembly, and provides an additional *de novo* assembly to be used in error correction. Using Saphyr, two mammalian genome maps can be created in a single run, for a total reagent and consumables cost of less than $2000 – a fraction of the sequencing and scaffolding cost for the entire project described in this paper, which approached $100,000.

The generated assembly, ARS1, represents an approximate 400-fold improvement in genome continuity due to properly assembled gaps compared to the previously published goat assembly, and better resolves the full structure of large repeats longer than 1 kilobase (kb). ARS1 comprises just 31 scaffolds and 649 gaps covering 30 of the 31 haploid, acrocentric goat chromosomes (excluding only the Y chromosome), which compares favorably to the current human reference (GRCh38), which has 24 scaffolds, 169 unplaced or un-localized scaffolds, and 832 gaps in the primary assembly.

The researchers concluded that the assembly strategy using multiple complementary technologies achieved superior continuity and accuracy, is cost-effective compared to past finishing approaches, and sets a new standard for mammalian genome assembly quality.

The Bionano Access software, which includes two-enzyme hybrid scaffolding and related scaffold editing, will be released as a free download later this month.

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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