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CORPORATE PRESENTATION

April 2019

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Opportunity

- Unique, proprietary sequencing platform (tSMS) for rapid growth billion dollar market
- \$5.3B addressable market for DNA and RNA sequencing by 2025
- Proven technology (10+ years R&D) across diverse genomic applications
- Currently engaged in multiple research projects for scientific discoveries
- Company primed for broad market commercialization

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Next Generation Sequencing (NGS)

- DNA stores hereditary information, static in nature
 - May provide information about susceptibility to disease
- RNA stores cellular information, dynamic in nature
 - RNA sequencing delivers "real-time" information to advance the understanding of biology





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TIRF Illumination Enables Single Molecule Resolution Imaging



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Massive Parallel Sequencing by Synthesis – a tSMS Advantage



Millions of individual molecules on the flow cell surface can be identified and resolved repeatedly through many rounds of nucleotide Incorporation to build the sequence of each strand.



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tSMS Captures Data Lost by Other NGS Platforms



- SeqLL tSMS efficiently sequences molecules of any length
- Short or degraded DNA/RNA
 - miRNAs
 - FFPE material
 - Forensic samples
- Micro RNAs are challenging to sequence due to their short length
- More complete analysis and greater depth of coverage
 SEQ Description

tSMS Offers Superior Signal-to-Noise for Detection of Subtle Changes

- <u>Cap Analysis of Gene Expression (CAGE) captures</u> mature, capped RNA species
- SeqLL (tSMS CAGE) measures full transcriptome with high accuracy, reproducibility and minimal bias
- Greatly improved signal-to-noise ratio compared to standard CAGE protocol
- Unprecedented detection of low-fold changes in gene expression
- Ability to correlate subtle changes in gene expression with health status for biomarker discovery, patient stratification and disease monitoring



Direct comparison of SeqLL tSMS CAGE protocol to standard CAGE protocol demonstrates higher correlation and lower standard error on the SeqLL platform

Reference: Kawaji, et al (2014) Genome Research (24)708-717

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tSMS Yields Greater Sensitivity and More Information

- ► SeqLL tSMS[™] identifies very lowexpression transcripts missed by the PCR-based method
- 7-fold better detection of low abundance transcripts
- 5-log linear dynamic range
- Superior tool for biomarker discovery and diagnosis



A Comparison of Single Molecule and Amplification Based Sequencing of Cancer Transcriptomes

Lee T. Sam^{1,2,3}, Doron Lipson⁴, Tal Raz⁴, Xuhong Cao^{1,5,6}, John Thompson⁴, Patrice M. Milos⁴, Dan Robinson^{1,5}, Arul M. Chinnaiyan^{1,5,6,7,8}, Chandan Kumar-Sinha^{1,5}, Christopher A. Maher^{1,2,5} 11

tSMS requires Simple Sample Preparation

Streamlines workflow to minimize manipulation bias and sample loss

- Does not utilize PCR amplification
- Avoids complex library prep
- Less restrictive nucleic acid quality requirements and no spec for GC content

Molecules of DNA or RNA are prepared for sequencing by:

- Standard nucleic acid isolation from any sample type
- Shearing/cleaving to appropriate length (20-500bp)
- Addition of Poly-A tail
- Hybridization to flow cell surface
- Sequencing individual strands by synthesis

Simple Sample Preparation – DNA



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Simple Sample Preparation – RNA



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52 Simple Sample Preparation – Direct RNA Sequencing (DRS°)

Flow Cell Surface

tSMS Requires Few Steps During Sample Prep 16

SeqLL technology



The tSMS Advantages – More Accurate, Sensitive & Cost-Effective

- Rapid, scalable, low cost sample preparation
- No amplification step means higher accuracy, sensitivity and predictive value
- Picogram DNA/RNA material yields millions of sequence reads
- Direct RNA sequencing is first developed on SeqLL platform
- Direct capture allows analysis of a set of target genes with minimal sample prep and high depth of coverage



tSMS Application Areas and Customers





Representative NGS Market Landscape

	ONANOPORE	SEQ	
ion	BIOSCIENCES"	<i>y</i>	
Resolut			
	iontorrent by Thermo Fisher Scientific	illumina" NextSeq 550	
	Yield (Reads,	/Run)	
			SEQ 🖁 LI

SeqLL Revenue Generation





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Management Team

- Daniel Jones CEO, President & Co-Founder 15 years in biotechnology sector, including 7 years at Helicos BioSciences developing applications for the tSMS technology platform. Co-inventor of Direct RNA Sequencing (Nature, 2009) and Single-Molecule Decoding of Combinatorially Modified Nucleosomes (Science, 2016). Mr. Jones has worked at U.S. Genomics on the development of their Trilogy 2020 Single Molecule Analyzer and Direct miRNA assays and at Exact Sciences on ColoGuard, a non-invasive, FDA-approved molecular diagnostic for colorectal cancer. Mr. Jones serves on the Board of Directors.
- John W. Kennedy, MBA CFO Finance executive with 34 years experience in finance and management. Worked at The Federal Reserve Board, Peat Marwick Mitchell (KPMG), Morgan Stanley & Co., and D.H. Blair & Co. Extensive investment banking expertise especially in small-caps, including roles as CFO & COO, and Managing Principal for US Broker-Dealers.
- Erik Volke Director of Operations Expertise in Manufacturing, Quality Assurance, and R&D. He has over 16 years' experience in manufacturing biotechnology and medical device instrumentation at Affymetrix, Helicos Biosciences, Life Technologies and T2 Biosystems where he has held manufacturing and quality management positions at both start-up and established FDA regulated ISO 13485 environments.
- Abhijeet Shinde, MS Director of Engineering Brings over 12 years' experience in developing biotechnology and medical device instrumentation, and developing products from concept to commercialization in FDA regulated ISO 13485 environments. More than 7 years of direct experience with single molecule sequencing at Helicos Biosciences where he lead system integration efforts.
- William St. Laurent, Chairman, Investor and Co-Founder Founder of numerous companies in diverse economic sectors. Mr. St. Laurent has over thirty years of experience in leading growth companies, developing and executing strategy, including building businesses from the ground up. Serves on the Board of Directors of the St. Laurent Institute and Genomic Diagnostic Technologies, both focusing on technologies in Systems Biology. Mr. St. Laurent is the Chairman of the Board of Directors.



Case Studies – Summary of tSMS Applications 23

- Identified biomarkers used as a gene panel for pancreatic cancer screen test
- Identified biomarkers used as a gene panel for CAD Risk Assessment
- Custom implementation of BRCA1 mutation detection and identification
- Effective information generation from degraded FFPE samples
- Pathway changes identified by high-sensitivity differential gene expression analysis



Case Study #1 – Screen Test for Pancreatic Cancer

- HSATII Satellite Overexpression for early detection of Pancreatic Cancer
- Discovered using tSMS technology
- Detectable ONLY with single molecule sequencing technology



Pericentromeric satellite repeat expansions through RNA-derived DNA intermediates in cancer

иненна внаме, виднов и била С. Маквенске, вида W. Science. 2011 February 4; 331(6017): 593–596. doi:10.1126/science.1200801.

Aberrant Overexpression of Satellite Repeats in Pancreatic and Other Epithelial Cancers

CrossMark

David T. Ting^{1,*}, Doron Lipson², Suchismita Paul¹, Brian W. Brannigan¹, Sara Akhavanfard¹, Erik J. Coffman¹, Gianmarco Contino¹, Vikram Deshpande¹, A. John Iafrate¹, Stan Letovsky², Miguel N. Rivera¹, Nabeel Bardeesy¹, Shyamala Maheswaran¹, and Daniel A. Haber^{1,†}

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Discovery of Novel Biomarkers

Detect signals not resolved by other NGS platforms

- Genes with 1.3 to 1.5 fold change identified and investigated
- Panel of 7 transcripts identified as highly predictive risk markers
- Diagnostic assay for clinical use under development



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tSMS Outperforms the Clinical Model

- Standard of care clinical model based on 7 indicators has very low positive predictive value (41.7%)
- tSMS platform based on 7 transcripts has a far superior positive predictive value (85.4%)



Case Study #3 – Direct Capture Sequencing (BRCA1)

Direct Capture Oligos Spanning BRCA1 Gene



- Capture primers are designed to span regions of interest in one or more genes
- Primers are deposited onto flow cell surface
- Isolated DNA/RNA is loaded directly onto flow cell without further manipulation
- Captured sequences are sequenced by synthesis



Direct Capture Sequencing – BRCA1

Deep Coverage of Targeted Regions



Direct Capture Sequencing – BRCA1

Target Enrichment from Genomic DNA



Direct Capture Sequencing – BRCA1

Successful Proof-of-Principle



Case Study#4 – FFPE-RNA Cancer Diagnostics 32



- RNA-Seq detects known gene fusions, SNPs, and mutations in NSCLC.
- SeqLL short read platform is optimal for sequencing of degraded FFPE samples.
- Potential to unlock 1000s of clinical specimens for R&D and future diagnostics.

Case Study #5 – Drug Mechanism of Action Analysis

Epidermis development gene subnetwork

- Transcriptome profiling identified drug activity on genes and pathway(s) related to wound healing
- Time course demonstrated that cell motility is increased by drug, which facilitates wound healing

Summary of Applications & Case Studies

Pharmacogenomics and Biomarker discovery

- Clinical Trial Screening Biomarkers
- Patient Stratification
- Companion Diagnostics

Microbial Analyses

- Microbiome Sequencing
- Antimicrobial Resistance Detection/Monitoring
- Food Safety Testing
- Forensics

Precision Medicine

- Early Disease Detection/Diagnosis
- Infection/Inflammation Differentiation
- Direct Capture Gene Sequencing
- FFPE Sample Analysis
- Cell-free DNA and RNA

Summary of tSMS Technology

- <u>A superior tool</u> for biomarker discovery, diagnostic development and sample analysis
- Unique features open up new capabilities not possible with other NGS technologies
 - Unsurpassed accuracy and reproducibility of molecule counting
 - Enhanced signal to noise allows identification of subtle gene expression signatures detectable on other systems
 - Lack of amplification and library prep produce the most unbiased read of the sample available in the industry today
 - Low sample prep costs and simplified workflow save time and money
 - Capable of generating data from short and degraded samples

Applications in a wide range of human disease areas, microbiome analysis, safety testing, forensics, clinical trial patient stratification and more

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