

Investor & Analyst Day November 20, 2024



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Investor Day Agenda

Management	Q&A Session	11:30 AM–Noon
Jeff Hawkins, CEO	The Proteomics Lab of the Future	11:20–11:30 AM
John Vieceli, CPO	Platform Roadmap	11:00–11:20 AM
Brian Reed, PhD	Innovating Discovery Applications in Proteomics	10:40–11:00 AM
Todd Rearick, CTO	Technology Architecture for the Future	10:20–10:40 AM
Jeff Hawkins, CEO	Proteomics Market: Current & Future Perspective	10:00–10:20 AM

Proteomics Market: Current & Future Perspective



Proteins are the Core of Biological Discoveries



Disease Biomarkers Therapeutic Development

Biotech Innovation

Proteins are the vital engines of biological systems, playing crucial roles in both health and disease



Transcriptomics Does Not Accurately Predict Protein Profiles



Disease Progression Goes Beyond the Protein Level



Proteomics is a Large and Growing Market Opportunity

\$8B+ Initial Target Market²

\$75B+ Proteomics Market¹



SVB Leerink Research, "Proteomics: The Next Frontier in Life Science Tools and Diagnostics." September 28, 2021
DeciBio Consulting Evaluation, June 2020

Platinum Use Cases Today

Identify Proteins Critical to Biology



In-gel digest of bio samples



Characterize antibodies



Identify co-IP proteins

Uncover + Understand **Proteoforms**

Post-translational modifications

Amino acid variants



RNA isoforms

Screen and Characterize Proteins with Barcodes



Protein/antibody engineering



mRNA vaccine development

Lipid nanoparticle delivery

How QSI Customers Are Leveraging Platinum



MRNA screening with protein barcodes for gene therapy



Studying citrullination PTMs



Characterizing far-flung extremophiles



Studying mRNA translation and PTMs



Studying disease isoforms



Mapping protein conformations using protein barcodes

The Proteomics Market is Poised for Significant Growth

Large-scale screening studies designed to identify clinically relevant biomarkers are

Deep proteoform-level analysis will be needed to

increasing

analysis will be needed to fully define and characterize the biomarkers with highest medical value



Population-scale studies will be needed to characterize what a "healthy" profile looks like





Routine use of multiomics

requires creating new data analysis tools — these tools will require large amounts of training data



Al-driven drug development

will drive the need for deeper proteomic data (amino acid level) to better inform and train the models



The proteome is dynamic

— longitudinal data will be needed (i.e., repeat testing)

Technical Challenges in Proteomics Today



Multiple Specialized Platforms Required to Fully Interrogate the Proteome



QSI is Best Positioned to Usher in a New Paradigm in Proteomics



Proteus[™]

Core technology is the only commercially available tech that can enable single-molecule, top-down, and bottom-up proteomics methods



New architecture (Proteus[™]), combined with other ongoing technology development initiatives, creates clear path to *de novo* sequencing



Ultrarapid sequencing chemistry can enable significant increase in sample throughput per day and unlock time-sensitive applications (e.g., clinical diagnostics) in the future

Platinum[®] Pro



Distribution Agreement in Place to Scale Adoption Across the US + Canada



	Sequencing Chip Kit	
Platinum' Pro	Sequencing Kit	Barcoding Kit
Querifican S	Library Prep Kit	Library Prep Kit





QUANTUM SI

Technology Development Pipeline

Quantum-Si Core Technologies

Platinum[®] System 2M Chip





Chemistry Biomolecules





Algorithms Applications



ထိုး။ **Barcode Applications**



Variant Calling

PTM Characterization



Protein Identification

End-to-End Protein Analysis



Prepare Proteins for Sequencing

Proteins are digested into short fragments (peptides)



Peptides are immobilized at the bottom of reaction chambers on our chip



Semiconductor chip

Kinetic Signatures Uniquely Identify Proteins + Proteoforms



Recognizers bind amino acids in sequence



Recognition events produce kinetic signatures







Rationale for New Technology Architecture



Semiconductors require large R&D investment



Re-partitioning of system allows for less expensive consumable



Leverage optical magnification to pack wells closer together and scale to billions of reads



Leverage high-performance, commerciallyavailable imaging components



QSI Core Technologies



Chip + Surface Chemistry

Simple passive device with approximately 20M wells (per flow cell) at initial launch



Heavily de-risked — leverages existing design, materials, and fabrication methods



Compatible with existing surface chemistry



Proteus[™] Consumable Development



Wafer process flow developed in production foundry



Prototype wafers fabricated and tested



Simple process has low-risk path to high-volume production



Wafer Fabrication Process Development



Foundry process modules work and produce the desired well structure



Foundry partner for development and production is in place



Proteus[™] Instrument Development



Move imaging components to the system



Increase workflow automation

Leverage commercially available technologies for imaging and liquid handling



Takes advantage of significant investment in optics driven by NGS industry



Library Prep + Sequencing Chemistry



Existing library prep and sequencing chemistry are completely portable



New system discriminates dyes with color rather than lifetime



Some new dye development is necessary, but is underway and low risk



Color Ratio is a Viable Alternative to Current Lifetime Detection





Move to color means we can leverage off-the-shelf camera technology



Analysis Software



Backend processing is completely portable to new system

• Pulse detection, ROI calling, alignment, protein inference, and other applications



Development required for frontend image processing



Well within state-of-the-art capability



Registration Deconvolution



Instrument Roadmap



New architecture scales up to 10B reads per consumable



Enables shotgun proteomics Proteus[™] 2.0 of complex samples QUANTUM SI (**10B**) 0 Platinum[®] Pro Puts us on path to Proteus[™] 1.0 de novo sequencing (**50M+**) Platinum (2M)

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Innovation Toward the Most Advanced Set of Discovery Applications in Proteomics

Brian Reed





Innovation at the Forefront of Proteomics

- The path to complete proteome coverage
- **Ultrasensitive PTM detection for proteoforms**
- Deep, unbiased interrogation of high-complexity samples
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Beyond sequencing: the first platform for top-down single-molecule proteomics



Acceleration on the Path to Complete Proteome Coverage

Sequence Proteins on Platinum



- Each recognizer binds 1-3 cognate N-terminal amino acids (NAAs)
- Rapid on-off binding generates a pulsing pattern detected by the chip
- Extremely information-rich data output: 10s-100s of pulsing events per amino acid

A Rapid Path to Complete Amino Acid Coverage

Our team has mastered the engineering and evolution of amino acid recognizers

Recognition Progress





- As a result of our rich kinetic output, we have more data on our recognizers than possibly any other set of proteins in biotechnology
- Recognizers in the V3 kit recognize 13 of the 20 types of amino acids (69%)
- New recognizers have already been developed and are on track for release in our next kit update
- We are on track to enable complete reference-free sequencing: enables key applications like sequencing antibodies and cancer neoantigens de novo
Kinetic Signatures are Sensitive to Downstream Sequence



- Recognizers physically contact residues
 downstream of bound NAA
- Influence is encoded in the peptide's kinetic signature and is highly predictable
- Kinetic signatures are a unique and powerful feature of Quantum-Si's core technology
- The acquisition of single-molecule kinetic information gives us unprecedented insight into binding interactions



Ultrasensitive PTM Detection for Proteins and Proteoforms

Phosphorylation is the Most Abundant PTM in the Human Proteome



Nat Chem Biol 14, 206–214 (2018). https://doi.org/10.1038/nchembio.2576

- Post-translational modifications (PTMs) are central to protein function and implicated in human diseases
- There are more than 400 different types of PTMs; phosphorylation is the dominant type (~72% of all PTM sites)
- Phosphorylation has the largest disease association: 81% of all discovered PTMassociated diseases¹

Affinity Reagents as Ultrasensitive PTM Recognizers



- Anti-PTM antibodies and other affinity reagents work on chip for ultrasensitive PTM detection
- Deliver the same real-time kinetic information as NAA recognizers
- Recognize PTMs anywhere in the peptide (not just at the N-terminus)

AQRYLAYPE

Affinity Reagents as Ultrasensitive PTM Recognizers



- **Step1:** PTM detection for 30 minutes with PTM recognizer
- Step 2: Normal protein sequencing with NAA recognizers
- PTM recogizers can be multiplexed and combined with kinetic signatures to pinpoint PTMs in multisite configurations

Ultrasensitive Phosphotyrosine Detection with CDNF

CDNF_HUMAN

..QEAGGRPGADCEVCK EFLNRFYK SLIDRGVNFSLDTIEK ELISFCLDTK..



Detection of less than 1 PTM-modified peptide in 1,000

- Extreme sensitivity to PTM stoichiometry due to the clear pulsing pattern from PTM recognition
- Example: a CDNF peptide is detected at a ratio of less than 1 phosphorylated peptide in 1,000
- Method can be extended to other types of PTMs, e.g., ubiquitination, glycosylation; works with commercially available affinity reagents

Recognition of Human TAU Proteoforms

TAU_HUMAN

...VAVVRTPPKSPSSAK **SRLQTAPVPMPDLK** NVK SK IGSTENLK HQPGGGK VQIINK K..



- Affinity reagents can be used in a bottom-up or top-down configuration
- **Example:** bottom-up recognition of pT* on human TAU peptides, top-down detection of immobilized full-length TAU proteoforms
- Real-time approach enables proteoform detecting reagents to be run simultaneously
- First commercially available platform for detection and differentiation of full-length proteoforms



Unbiased Interrogation of High-Complexity Samples with Quantum-Si's Core Technology

Sequencing Complex Biological Samples Unlocks Broad Access to Proteomics



- **Biological samples like serum** contain hundreds to thousands of proteins with wide dynamic range of abundance
- Unbiased, consistent, accessible interrogation of these samples is a challenge in proteomics
- Sequencing is not limited to predefined content: enables discovery of changes in proteins and proteoforms that other methods are unable to access

Unbiased Interrogation of High-Complexity Samples



- New chip architectures and advances in sequencing chemistry will enable sequencing biological samples at ever-increasing depth
- Future versions of the platform will see shotgun sequencing with thousands of proteins identified
- **Barcoding approaches** and flowcell designs will enable sample multiplexing
- Innovative methods to fractionate proteins and to reduce sample complexity will be combined with these improvements

Fast Sequencing for Deep Coverage and Rapid Sampleto-Answer



- We have developed new sequencing chemistry with a much faster rate of sequencing
- With FAST chemistry, we achieve equal performance to 10-hour runs in just 90 minutes (version 1)
- Path to runs <30 minutes for some applications with further development
- Enables deep sample coverage via iterative FAST sequencing and rapid sample-to-answer methods for clinical applications



Beyond Sequencing: the First Commercially Available Platform for Top-Down Single-Molecule Proteomics

Detecting Antibody Binding Events with the Power of Real-Time Kinetics

Dye-cycling enables ultrasensitive real-time detection of biomarkers



- Detection of fixed protein panels with high sensitivity is an increasingly important application in proteomics
- We developed a single-molecule sandwich assay that enables real-time detection of biomarkers
- Dye-cycling approach uses our existing kits to translate immune complex formation into a readily detected pulsing segment

Ultrasensitive Detection of Proteins in Serum

Direct detection of proteins in serum with high sensitivity



Spike-in titration experiments in serum demonstrate 0.1–1 pg/mL detection (path down to 10 fg/mL with further development)

Multiplexed Ultrasensitive Protein Biomarker Detection

Multiplexed detection of human IL6 and TNF- α



- Affinity reagents against multiple biomarkers can be loaded on the chip
- Dye-cycling approach enables discrimination of biomarkers by fluorescence and kinetic properties in multiplexed assays, along with PTMs

A Platform for Ultrasensitive Detection of Protein Panels

IL10 IL6 IL2 IL4 TNFα **IFNy IL12** Protein panel size scales with the platform <u>c</u> ProteusTM 2.0 (1,000+) Э Э Proteus[™] 1.0 (100's)Platinum (up to

Multiplexed biomarker detection directly in serum

- Sensitivity on Platinum is suitable for commercialization of panels with up to 10 proteins
- Panel size scales with the platform, as well as capacity to multiplex samples
- Proteins detected directly in serum on chip, eliminating complex sample prep
- Sample-to-answer in ~2 hours with one instrument

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Platform Roadmap

Nov 20, 2024

John Vieceli



Innovation Pipeline is Robust and Accelerating



Sequencing Analysis Software



Software Workflows for Next-Gen Protein Sequencing™



Protein Inference

Kinetic signature enables inference of sample protein from whole human proteome panel

Rank	Inferred Protein	Score	Likelihood	Mass (kDa)	Length
1 IL4	4 spIP04112IIL4_HUMAN	11.035496	99.99%	17	153
2	spIP06127ICD5_HUMAN	0.593929	44.78%	55	495
3	spIQ15208ISTK38_HUMAN	0.582068	44.12%	54	465
4	splQ96LQ0IPPR36_HUMAN	0.506878	39.76%	49	422
5	splQ81WR1ITRI59_HUMAN	0.440162	35.6%	47	403
6	spIQ9UMR3ITBX20_HUMAN	0.428596	34.85%	49	447
7	splQ96EU6IRRP36_HUMAN	0.403635	33.21%	30	259
8	splQ9H2F9ICCD68_HUMAN	0.371386	31.02%	39	335
9	spIQ8IVI9INOSTN_HUMAN	0.365859	30.63%	58	506
10	spIO9BZ81IMAGB5_HUMAN	0.310895	26.72%	32	275

ProteoVue™ Variant Calling

Kinetic signature enables differentiation of protein variations at the single amino acid level



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Artificial Intelligence

N-terminal Amino Acid Recognizer Development





Recognizer Protein Design Al







Amino acid recognizer **backbone design**

Amino acid recognizer sequence design

Orthogonal verification of amino acid recognizer protein design



Pulse Width Prediction Using Artificial Intelligence



Platinum Sequencing

QSI is continually increasing the size of the training data with more proteins and/or new binders



Pulse Width Prediction Al

Currently predicts ~4.6 million pulse widths used in analysis



Better Performance

Pulse width prediction Al trained with more platinum sequencing data improves protein detection performance

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Platinum[®] Pro

Platinum[®] Instrument





Customers identified opportunities to improve workflow and UI/UX



Functionality limited to protein & peptide sequencing



Local analysis enabled by additional server

Introducing Platinum[®] Pro





Streamlined workflow and reduced hands-on time



Pro Mode enables new applications

Onboard analysis or via the cloud

(h)

Enhanced user interface



Streamlined Workflow Improves Usability



Pro Mode Available only on Platinum Pro







Peptide Barcodes can be Used to Monitor Protein Expression Both *In Vivo* or *In Vitro*



Equimolar 5 barcode mix encoded as mRNA and packaged into LNPs



Inject into mouse model; harvest target tissues



Enrich for target protein, functionalize, cleave, and sequence barcodes





V2 Library Preparation Kit Improvements





Simplified workflow reduces need for buffer exchange



Improved performance with ~80% of proteins successfully inferred



Reduced protein input five-fold



Proteus[™] Increases Throughput + Automation





Switch from semiconductor to optical architecture with patterned array for throughput scalability



Liquid handling automation simplifies workflow and reduces hands-on time



Up to an order of magnitude throughput increase per sample relative to Platinum at initial launch

Proteus[™] Increases Number of Samples

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Run one or two samples simultaneously



Reagent cartridges with sequencing workflow automation



Run up to 8 samples in one sequencing run



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The Proteomics Lab of the Future



QSI's Pipeline is Heavily De-risked Compared to Other Proteomics Companies



Builds upon QSI's existing commercially available technologies



Industry-leading protein and enzyme engineering program operating at scale and with high success rates



Manufacturing infrastructure in place and routinely producing and delivering product to customers today


Strategic Partnerships to Accelerate Commercial Adoption and Deliver on Innovation Roadmap









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QSI is Best Positioned to Usher in a New Paradigm in Proteomics



New platform architecture designed so QSI will not be feature limited (can scale to billions of reads)



QSI core technology is the only commercially available tech that can enable single-molecule, top-down, and bottom-up proteomic analysis



QSI ultrarapid sequencing can enable significant increase in sample throughput per day and unlock time-sensitive applications (e.g. clinical diagnostics) in the future



QSI new architecture, combined with other ongoing technology development initiatives, creates clear path to *de novo* sequencing

QSI Near-term Pipeline Will Unlock Opportunities Across All Market Segments



Proteomics Lab Today



Many specialized platforms needed to fully interrogate the proteome



Technical tradeoffs when selecting between the breadth of protein coverage and depth of insights



High capital costs and manual workflows limit the number of laboratories capable of performing proteomics



QUANTUM SI

QSI Will Power the Proteomics Lab of the Future



One platform and core technology capable of addressing the broadest range of proteomics analysis methods



Eliminate technical tradeoffs – single-molecule, amino acids and PTMs, top-down or bottom-up, ultrasensitive, scalable throughput



Affordable and automated, allowing any lab — anywhere — to be a proteomics core lab



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