Evanescent Planar Waveguide Technology

In order to appreciate the power and uniqueness of Brava's evanescent planar waveguide technology, it is helpful to understand the evolution of technologies used in medical diagnostics, especially in the context of measuring substances that are present in the blood at very low concentrations.

1. Immunoassays start with a capture antibody that is bound to a substrate. The antibody is specific to a target analyte (e.g., a protein or foreign substance).
   - When the sample is introduced to the test system, the target analyte is captured by the antibody.
   - A second antibody conjugated with a detector binds to another part of the target analyte.
   - The amount of detector is measured, which correlates to the concentration of the analyte.

2. By the 1980s, common substrates used in central lab immunoassays included glass cuvettes, plastic microtiter plates and magnetic beads.
   - Detectors include colorimetric, fluorescent, luminescent or electrochemical signals.

3. Direct fluorescence and chemiluminescence assays can measure very low concentrations of analytes. These lab instruments are complex and have expensive fluidics and detection modules.

4. There are research platforms available today that can detect single molecules.

5. Point-of-care technologies, such as lateral flow assays, were developed using membranes as substrate and colloidal gold in the detection system (e.g., pregnancy, strep A POC tests).
   - Silicon chips were combined with enzymatic assays with electrochemistry detection (iSTAT).
   - BioSite (now part of Quidel) innovated a lateral flow method with fluorescence measurement with a small meter.
   - Waveguide technology development began in the 1990s using thin film and glass slides. While the technology was proven to be extremely sensitive, it was too expensive to commercialize as an IVD product.

6. Microfluidics POC technologies began to emerge in the 2000s. (OPKO and others)

7. MBio developed assays using injection molded plastic waveguides with an integrated lens. This cost-effective innovation was enabled by new, optically pure plastics.
   - MBio developed a low-cost reader that leverages consumer imaging electronics.
   - Brava will extend MBio's accomplishments and develop a high-sensitivity troponin assay.
Our Technology
Evanescent planar waveguide technology enables rapid and quantitative measurement of very low concentrations in whole blood. This combination is critical in acute care settings, where precision at low concentrations is imperative to drive treatment decisions.

Instrument
Instrument development has been de-risked through ten years of investment.

The LightDeck System offers these advantages:
- Analytical sensitivity: Delivers precise results at pg/mL levels, comparable to the central lab.
- Rapid, simple format: Whole blood assays report results in less than 15 minutes using an easy “load-and-go” workflow.
- Multiplexing: Multiplexing improves precision.
- Cost-effective: The design of the disposable cartridge is scalable and enables commercialization with high margins.

Planar Waveguide
Planar waveguides have been incorporated into low-cost, disposable, injection molded plastic cartridges. The printed microarray has multiple spots per analyte for better precision and positive and negative controls to improve quality and safety. This simple format may earn CLIA waiver.

Light is focused through an integrated lens and bounces through the plastic to create an evanescent field just above the waveguide. This evanescent field excites only the fluorescent dye that is bound by the capture antibody on the waveguide. The evanescent field is like a “glowing floor” and eliminates noise associated with blood components and detection reagents that are not bound to the waveguide.

The spots are imaged and the fluorescence is quantified by a CMOS camera, similar to a cell phone camera.

Intellectual Property
The core technology is protected by 10 issued U.S. utility patents (earliest expiration is 2032), 5 issued U.S. design patents and 14 issued international patents in Europe, Asia and South Africa. IP covers Waveguides (core platform technology), Fluidic Assay Cartridge and Processing Methods, Multiplexed Assay System and Cell Counting System.

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