Cyto-Mine®: Single cell analysis and monoclonality assurance system for B-cell and Hybridoma screening

Corporate:

Sphere Fluidics Ltd, an established Life Sciences company based near Cambridge (UK), develops unique products for use in single cell analysis and characterisation and provides collaborative R&D services. The Company has 54 patents (12 patent families with 25 patents being granted) and over 140 international customers. To enable a step-change in the way the biopharmaceutical industry finds and isolates rare cells producing biologics of interest, Sphere Fluidics is currently developing Cyto-Mine®, the single cell analysis and monoclonality assurance system.

Key Application Areas:

- **Biopharmaceutical Discovery:** Isolation, assaying, sorting and dispensing of individual B-cells or hybridomas based on antigen specificity.
- **Bioprocessing:** Analysis of heterogeneous cell populations for identification and cloning of the highest-secreting single cells.
- **Quality Assurance:** Allows ongoing analysis of working cell lines to detect early onset of potential genetic drift of bulk cultures.

Advancing the Discovery of Monoclonal Antibody Biologics:

Sphere Fluidics has developed unique technology to enable a step-change in the way the biopharmaceutical industry finds and isolates antigen-specific B-cell and hybridoma clones. Using proprietary picodroplet technology and microfluidics, the platform compartmentalises cells into individual aqueous picodroplets. Each picodroplet is analysed and sorted, and only those containing a single cell producing antigen-specific monoclonal antibodies are collected to wells of microplates. In a few hours, the platform can analyse antibody production from up to a million primary B-cells or hybridomas. The platform will deliver significant savings in time and consumable costs with greater statistical accuracy in rare cell recovery.

System Features:

- Processes up to 1 million B-cells or hybridomas in less than half a day.
- Directly assays each individual cell for antigen-specificity in culture medium environment.
- Multiplex assay system permits screening based on multiple parameters.
- Isolates up to 5,000 antigen-specific single cells into individual wells with high viability.
- Single-use, disposable flow pathway ensures sterility and minimal turnaround time.
- Benchtop system compatible for use in Class II biosafety cabinet.

Primary B-Cell Analysis:

- **Cyto-Mine® (Phase C)**
  - Analyse ~ 10⁶ primary B-cells in a few hours.
  - Single cell dispensing - Monoclonality Assurance
  - Sterile workflows in self-contained Cyto-Cartridges™
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Manual / Limiting Dilution</th>
<th>Automation / Clone Pickers</th>
<th>Flow Cytometry / FACS</th>
<th>Picodroplets / Cyto-Mine®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Throughput/Run</td>
<td>1,000</td>
<td>10,000</td>
<td>&gt; 1 billion</td>
<td>Up to 1 million</td>
</tr>
<tr>
<td>Time Per Run (days)</td>
<td>90</td>
<td>21</td>
<td>1</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Monoclonality Efficiency (%)</td>
<td>8 - 40</td>
<td>95.6</td>
<td>98 to &gt; 99</td>
<td>&gt; 99.9</td>
</tr>
<tr>
<td>Single Cell Compartmentalisation</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>In-Line Assays</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Single-use Disposable Flow Path</td>
<td>Yes</td>
<td>No</td>
<td>Yes/No</td>
<td>Yes</td>
</tr>
<tr>
<td>Cell-cell Interaction Studies</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Optical analysis and Verification</td>
<td>No</td>
<td>Yes/No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Low Shear Forces</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Detects Low-abundance, Cell-Surface Proteins on a Single Cell (using enzyme amplification)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>High Accuracy</td>
<td>No</td>
<td>Yes/No</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Small Footprint/Size</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Sample Environment Sterility</td>
<td>n/a</td>
<td>Yes</td>
<td>Yes/No</td>
<td>Yes</td>
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<tr>
<td>Enables Single Molecule Assays</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Cyto-Mine® Technology Access Program:

- Early access to this leading-edge, disruptive technology will provide the Technology Access Partner with:
  - Reductions in operational costs, time and resource.
  - Significant advantages over competitors.
- Provides opportunity to help shape the product platform to better meet specific, operational requirements.
- Product development costs are shared over a small number of Partners, providing significant cost savings.
- Each Partner gains early access to the instrument platform, Cyto-Cartridges™, specialist chemicals, patent licenses, technical and application support.
- The program includes upgrading of an early (or alpha) version to a full production system.
- Partners receive ongoing discounts on future purchases of instruments and consumables.

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