Sphere Fluidics Ltd.

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Cyto-Mine: single-cell-analysis technology reinventing therapeutic discovery

Assisting biopharmaceutical drug discovery and development, particularly with regard to monoclonal antibodies, Sphere Fluidics has developed an integrated platform capable of processing, assaying, sorting and dispensing single cells.

S phere Fluidics has reached an inflection point in its development. Having spun out of the University of Cambridge in 2010, Sphere Fluidics has now built up the resources, collaborators and capabilities to realize its ambition of revolutionizing therapeutic discovery and development through the application of singlecell analysis and engineering.

The company has timed its evolution well. Sphere Fluidics began by commercializing biochips, specialty chemicals and other consumables to support the processing of millions of individual single cells in picoliter-sized compartments called picodroplets. That enabled the business to gain knowledge of novel applications and generate income while advancing its technology. In parallel, Sphere Fluidics delivered successful R&D collaborative programs to international clients, raised investment and moved into new, custom-designed laboratories in the scientific hotbed around Cambridge, UK.

Now, with biopharma companies pushing hard to improve their monoclonal antibody (mAb)discovery and cell-engineering capabilities, Sphere Fluidics is preparing to roll out high-value systems that meet these very needs.

Cyto-Mine: a problem solver for mAb researchers

The centerpiece of the latest evolution of Sphere Fluidics' product range is Cyto-Mine, an integrated platform for the processing, assaying, sorting and dispensing of single cells (Fig.1).

This system can be used for biotherapeutic discovery and development (e.g., the detection of secreted proteins such as antibodies), the engineering of single-cell therapies for personalized medicines, and even diagnosis of disease markers at the single-cell level. Isolating and studying single cells can enable the visualization

Sphere Fluidics has already signed up several biopharma companies to its technology access program and is on the cusp of adding more. of subtle differences in, for example, cancer cell subpopulations in a biopsy and thereby simplify the selection of a precision medicine for the patient.

In the biopharmaceutical sector, drug discovery teams currently rely on a patchwork of technologies, such as automated clone pickers, imagers, robotics and flow cytometers, to carry out their research activities. Before Cyto-Mine, no single system could handle the ultrahigh-throughput screening, single-cell assays, and rapid sorting and dispensing of 'hits' into individual wells of a microtiter plate that are required for the workflow of a mAb drug discovery and development operation. Cyto-Mine draws on Sphere Fluidics' expertise in the handling of picodroplets and microfluidics to provide a fully automated, integrated 'load-and-go' system.

Cyto-Mine creates picodroplets to compartmentalize single cells in a small-footprint machine and can perform millions of single-cell or cellcell co-incubation assays per day. The focus is on eliminating the bottlenecks inherent in mAb discovery today. Sphere Fluidics designed the system after interviewing 30 organizations, liaising with regulators and seeking advice from independent experts. This collaborative approach is continuing with its technology access program. Sphere Fluidics has already signed up several biopharma companies to the program and is on the cusp of adding more.

Such collaborations enable Sphere Fluidics to pair its in-house expertise with feedback from the end users based in international biopharma discovery teams. Sphere Fluidics has also been successful in joining a leading syndicate including a major biopharma company, a contract manufacturing organization, a genome-editing company and other organizations to create a revolutionary approach for an 'advanced biologics manufacturing supply chain'. This project has a budget of over £11 million and is supported by UK government funding.

Single-cell engineering: where Sphere Fluidics is heading

As the success of Cyto-Mine grows, Sphere Fluidics is also aiming to accelerate growth by raising venture capital. Such funds will be used to establish Cyto-Mine as the leading platform for single-cell analysis in biologics drug discovery, development and manufacturing. Sphere Fluidics also has its eye on the next big market it wants to disrupt: single-cell engineering to create highquality precision therapies.



Figure 1: The Cyto-Mine system performs single cell analysis and monoclonality assurance workflows.

The company believes that by applying its expertise in the independent manipulation of millions of single cells, it can dramatically improve the workflow for researchers in the field. The plan is to create a technology platform that allows researchers to individually transfect each cell with a controlled number of vectors or viruses, or even with a single molecule. This would mitigate the current problems observed with bulk cell transfections, in which cell-engineering efficiencies are very low (e.g., <10%) and cells receive a nonuniform number of vectors, increasing the risk of cell mutation and oncogenicity. Such a system would revolutionize how researchers engineer T cells to create personalized cell therapies for cancer patients using their own cells. Sphere Fluidics is developing this platform with a syndicate of end users specializing in cell therapy.

If Sphere Fluidics can continue the sure-footed advance that has characterized its progress so far and fulfill its ambition to revolutionize cell engineering, it will find itself with key enabling technologies for two of the largest, newest fields in the pharmaceutical industry (biopharmaceuticals and cell therapies). The company has also identified other key markets and seems ideally placed to further enable the pharmaceutical industry to discover and develop improved therapies.

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