Introduction:

Cellomics® ArrayScan HCS System heralds a powerful paradigm shift in the target validation and lead optimization processes. This automated cell analysis instrument generates information-rich data regarding the effects of potential new drugs on various aspects of one or several cellular targets.

The ArrayScan HCS System is the world's first drug discovery instrument that performs automated High Content Screening, to reveal more relevant and richer biological information and provide reliable insight into the efficacy and toxicity of your drug candidates. Measurement of complex cellular responses of numerous whole cells in parallel provides you with additional knowledge that can be critical to accurately determine which targets to investigate and which lead compounds to pursue.

Overview:

The spatial and temporal interactions of molecules in the cell comprise a complex, interrelated system that regulates cellular activity. The introduction of chemical compounds to the network can have pronounced positive (medicinal) and negative (oncogenic, toxic, or disease causing) effects. A deeper understanding of the interaction and effects of synthetic and natural compounds on the cellular processes is critical to assessing the cellular effects of drug candidates.

The ArrayScan HCS System performs automated measurement and analysis of spatial and temporal events in cells. Knowledge of cellular events reveals more relevant and higher content information and provides reliable insight into the efficacy and toxicity of drug candidates. Measurement of complex cellular responses will provide additional knowledge that can be critical to accurately determining which targets to investigate and which lead compounds to pursue.

The ArrayScan HCS System's inverse optical path is optimized for performing rapid automated scans through the bottom of clear-bottom microplates. The system automatically focuses on a field of cells and acquires images at each selected fluorescence channel. The ArrayScan software identifies and measures individual features, activities and structures of cellular targets or organelles at the single cell level or as a population average over a field or well of cells, so that hundreds of cells are analyzed in parallel. The software then tabulates and presents the results automatically in user-defined formats. All of the raw data, including images of individual cells, are archived and available for inspection and analysis.

The system fits easily into your current laboratory and permits growth into higher-density array formats.

The ArrayScan HCS software provides for multicolor imaging, automated cell-based image analysis, and data management for archiving, analysis and creation of reports. An

intuitive, graphical user interface guides you through image acquisition, image analysis, data review and data reporting.
Data and images generated by the ArrayScan HCS System can be stored in either standalone mode with an integrated Microsoft® Access based database or via a client/server database connection to the Cellomics® Store data management system. The ArrayScan HCS System standalone mode database capabilities included with the ArrayScan HCS software organize the multicolor fluorescence data and images from a single ArrayScan Instrument in database files for reviewing and reporting.

An Integrated Solution
The ArrayScan HCS System comes with all the equipment necessary for extracting high content information from cell-based assays. The system includes image processing and cell analysis software that captures and extracts data from images using proprietary algorithms. Data and images are transferred seamlessly and automatically from the instrumentation to a storage device for reviewing. Remote viewing of results can be performed from a local workstation over a local network system.

Features:

- Automatically finds cell fields, sets exposures, focus and thresholds during plate scanning
- Quantifies multiple fluorescent signals on or in cells in clear-bottom microplates
- Eliminates fluorescent artifacts, identifies cell subpopulations and/or subcellular compartments
- Automatically converts raw image data into signal distribution, area, morphology, and activity measurements
- Processes data "on-the-fly" providing user-definable data view during scanning and instantaneous hit recognition
- Stores images and all data collected for each cell or cell field measured for later review
- Provides real screening capacity with fast screening mode, plate stacking and "walk away" operation
- Reveals specificity, cytotoxicity, and bioavailability information on all of your primary screen hits
- Measures changes in subcellular distribution and activity of proteins and other molecules; changes in cellular morphology; changes specific to cell subtypes in a mixed population; changes in cell-cell communication

Specifications:

Microplates
Clear bottom 96 or 384-well microplates. Contact Cellomics about compatibility with microplates from specific manufacturers.

Robotic Plate Stacker
For fixed endpoint assays, up to 80 microplates can be loaded into the robotic plate stacker. Software control automatically loads plates onto the ArrayScan System for unattended, continuous scanning.

Barcode Reader
Identified barcode labels persist throughout the data retrieval process, guaranteeing proper identification of microplates and associated data.

Illumination
1500 Hour White light (Mercury-Xenon) arc lamp provides a broad range of wavelengths for fluorescent dye excitation.

Standard Filter Sets
Four band filter set for acquisition of up to four different color channels in a single assay.

Camera
High-resolution, high sensitivity digital camera.

Optics
Several available magnifications.

Computer
High-end MS-Windows NT workstation with removable storage, accelerated video graphics, and monitor.

Printer
Color printer.

Dimensions
30"(w) x 30"(d) x 24"(h)

Weight
400 lbs.

Power Requirements
120 VAC and 1500 watts / 220-240 VAC (50 Hz)

Applications:

Cellomics, Inc.'s ArrayScan HCS Systems include application software that affords immediate and powerful screening capabilities, with the flexibility to customize assays easily and quickly. Each application comprises a collection of optimized algorithms that automate the extraction and quantification of assay-specific biological information from cell images collected on the ArrayScan HCS System. All applications share the common characteristics of being multiparametric and information-rich, yielding consistent and robust screening results with optimized signal to noise ratios.

Current Applications	**Future Applications**
Cytoplasm-Nucleus Translocation	Target Validation/ Orphan GPCR Characterization
Receptor Internalization and Trafficking	Subcellular Trafficking
General Screening Application (GSA)	Cell Cycle
Multiparameter Apoptosis 1	Cellular Morphology
Cell Viability	Microtuble Assembly/Disassembly/Disruption
Mitotic Index	Adipogenesis
Neurite Outgrowth	Angiogenesis
Cell Spreading	
Cell Motility	
Multiparameter Cytotoxicity 1	

Technologies:

High Content Screening (HCS) is multiplexed, functional screening based on high-resolution fluorescence imaging of multiple targets in the context of intact cells. The goal is to draw from expertise in the fields of fluorescent microscopy and cell biology to create a new set of screening tools aimed at the bottlenecks in drug discovery. Cellomics, Inc., has successfully combined fluorescent reagents and cell lines, automated imaging instrumentation, informatics and bioinformatics tools to create a turnkey system that:

- quantifies multiple fluorescent signals on or in cells in standard microplate formats
- automatically converts raw image data into signal distribution, area, morphology, & activity measurements
- automatically finds cell fields, sets exposures, thresholds, and focus during plate scanning
- eliminates fluorescent artifacts, identifies cell subtypes and /or cellular compartments

- processes data "on the fly" providing a user definable results display during scanning
- stores images (optional) and all data collected for each cell or cell field measured for later review or reanalysis
- provides real screening capacity with plate stacking and "walk away" operation

HCS has significant advantages over standard fluorescent plate readers used in cell based assays. Individual cellular measurements, as opposed to a single intensity read averaged over the entire well gives you the ability to:

- measure biological variability of the cells in your assay
- isolate and measure cell sub-populations or differential expressers
- locate and eliminate fluorescent artifacts and backgrounds

How does HCS generally apply to pharmaceutical industry needs?

1. HCS delivers the potential to screen using targets that were minimally used or avoided due to a lack of a robust way to measure them. Some examples include:
    - morphology changes, cellular differentiation and cytoskeletal changes
    - cell to cell interactions, chemotaxis, motility
    - spatial distribution changes like receptor trafficking or complex formation
2. The multi-parameter nature of HCS can be used to create specificity assays where two or more proteins (enzymes, factors, receptors, signals) or pathways can be simultaneously measured in individual cells in the well. Multiplexing can also be used to cross correlate measures of cell stress, organelle health, and cytotoxicity with primary measures on an individual cell basis.
3. HCS can extract additional valuable information from cells assayed in other fluorescent platforms, such as FLIPR®, where a calcium transient can be linked to downstream signaling events such as receptor internalization or measures of viability, morphology, apoptosis, etc.
4. HCS can be used diagnostically in conjunction with existing HTS Assays for quality control of cells, reagents, and assay preparation protocols. Evaluating stable clones and estimating expressed protein levels can also be addressed.

The HCS method enables more efficient validation of cellular targets, higher capacity for predictive toxicology and more effective lead optimization. The end result is decreased cycle times for drug discovery while increasing the probability of success in the clinic.

Informatics:

Cellomics® drug discovery platforms were developed to provide deep biological information (time, space, and activity) regarding multiple cellular targets in one or more disease-related pathways, and the physiological impact of new drug candidates within living cells. Such high content screening provides significant insights into the best targets to pursue while providing early understanding of the efficacy and toxicity of drug candidates. This knowledge assists in making informed decisions about compounds that are most likely to succeed in animal testing and human clinical trials.

Key components to our ArrayScan® HCS System are the accompanying informatics tools. Because high content screening produces vast amounts of information, the Cellomics informatics products automatically manage the storage and retrieval of all captured information in a reliable, intuitive, scalable, and cost effective manner. Furthermore, because the value of high content cellular information is fully realized only when presented in a manner appropriate for users to easily draw accurate conclusions, Cellomics has created a wide variety of flexible and exceptionally powerful tools for exploring, sharing, and visualizing your growing base of cellular knowledge.

The products profiled below are designed to work either independently or to build upon each other to enable users to make informed decisions during the early phases of drug discovery.

The Company's informatics tools provide a rich set of capabilities to manage and analyze complex cell-based data and associated images through a user-friendly visualization environment. This enables users to make informed decisions and provides transparent access to sophisticated analysis software and underlying large-scale databases.

Cellomics® Store
The Next Level in Data Management and Analysis for Cell-Based Screening
Cellomics Store builds upon the functionality of a variety of cell-based screening platforms including the ArrayScan® System by taking data management and assay analysis to the next level. With the addition of the Cellomics Store server platform, researchers are relieved of the burdens of data management and empowered with the resources to easily transform massive volumes of assay data into valuable information.

Cellomics Store provides:

- Visualization of data and analytical tools for cross-plate analysis.
- Visualization of results at the plate level and individual wells.
- Powerful "drill-down" capabilities automatically link data from plate-level, to well-level, to cell-level, all the way to the actual images of the cells acquired in multiple channels of fluorescence.
- Optimal storage and transparent access to the massive volumes of data and images that are produced by HCS. No more locating, sorting, and loading of archive media.

- Client/Server structure allows access to high content data from multiple Cellomics Store client PCs. Productivity is increased as information is distributed throughout your group.

Cellomics® Screen
Screening Process Management, Quality Control, Screen Analysis and Reporting
Cellomics® Screen adds another layer of screen management and analysis above Cellomics Store, providing tools for efficient management of the cell-based screening process. Cellomics Screen schedules and manages screening runs, in addition to retrieving, processing, and analyzing data from runs, and reporting results.

Cellomics Screen provides:

- Integrated support of high content screens, including parallel multi-parameter screening of multiple concurrent assays on every plate.
- Tools for creation and selection of assay protocols, plate layouts, compounds, controls, version information, etc.
- Graphical monitoring of screening runs across all plates in a run.
- Analysis of dose-response, IC50, percentage of control, etc.
- Cross-correlation of multiple parameters measured from all or selected plates in a HCS run.
- Powerful "drill-down" capabilities (via Cellomics Store) to automatically link data from screen-level, to plate-level, to well-level, to cell-level -- ultimately presenting actual images of cells measured using one or more channels of fluorescence