Automating Cell Biology

Annual general meeting, September 7, 2015

Phase Holographic Imaging

www.phiab.se

PHASE HOLOGRAPHIC IMAGING (PHI)

- Began as a research project at Lund University, Sweden, in 2000
- Founded in 2004
- Sales in 2014/15: 2.7 (1.4) MSEK
- Over 40 units in operation at customers and key opinion leaders
- 12 granted patents
- Number of employees: 11
- Publically traded since 2014
- Website: www.phiab.se

PHI leads the ground-breaking development of time-lapse cytometry instrumentation and software. With the first instrument introduced in 2011, the company today offers a range of products for long-term quantitative analysis of living cell dynamics that circumvent the drawbacks of traditional methods requiring toxic stains.

Headquartered in Lund, Sweden, PHI trades through a network of international distributors. Committed to promoting the science and practice of time-lapse cytometry, PHI is actively expanding its customer base and scientific collaborations in cancer research, inflammatory and autoimmune diseases, stem cell biology, gene therapy, regenerative medicine and toxicological studies.

WHAT IS CELL CULTURE?

- Experiments using cultured cells is the cornerstone of drug development and preclinical research
- Such experiments are the only opportunity to work on human cells before clinical trials
- In specialized cell laboratories, cells are artificially cultured in plastic containers inside a cell incubator

Cell culturing in a cell incubator

Cell culture preparation

CELL ANALYSIS

- To understand biological processes scientist study cultured cells using cell analysis, often after treating the cells with a drug
- Technical limitations of the past has led to that scientists predominantly observe cells when fixed and dead – *fixed cell analysis*
- *Live cell analysis* allows investigation of dynamic processes of living cells instead of only providing a "snapshot" of a cell's current state
- To characterize cellular behavior, cells are commonly *labeled* with chemicals or genetic modifications which emit light
- However, these labels are toxic and alter the natural behavior of cells
- Scientists therefore increasingly move to live cell analysis without using toxic labels, enabling repeated observations of the same cells over time – *label-free live cell analysis*

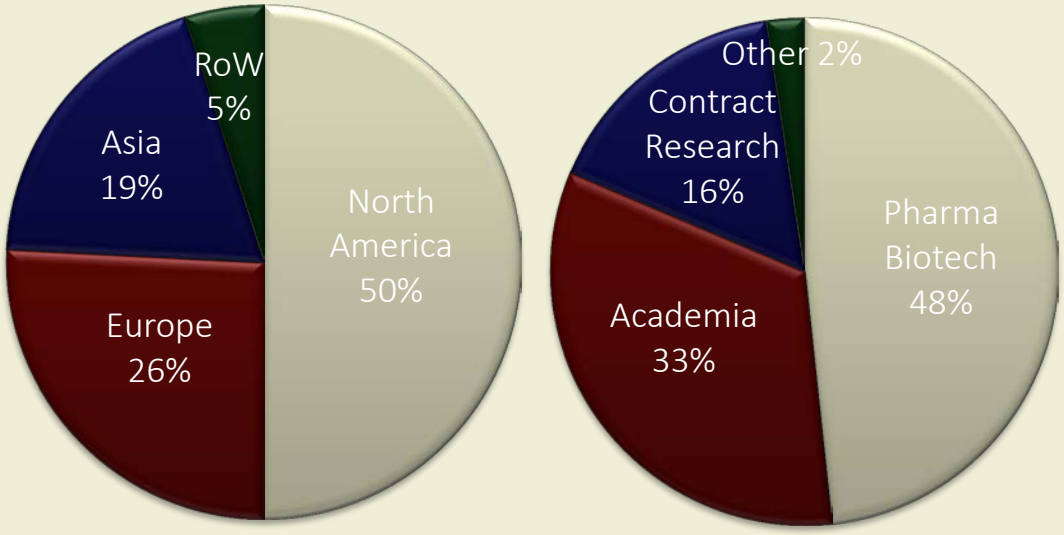
"Intoxicated humans do not display their natural behavior. The same applies to their building blocks – cells

MARKET SIZE

"Cell Analysis Flourishes Scientifically, Prospers Commercially"
Genetic Engineering and Biotechnology news, 2015

"The global market is estimated to be valued at $8.7 billion USD in 2013 and will grow at a CAGR of 11.1% from 2013 to 2018"
Cell-based Assays Market by Product, Application, End-user, Markets & Markets, 2014

Estimated number of labs performing cell analysis worldwide = 126 804
The Market for Cell-based Assays, Bioinformatics, gene2drug.com, 2015



Government initiatives and public-private partnerships along with drying drug pipeline in pharma industry have led to increase in drug discovery activities; which is stimulating the market growth. Presently, the market is all set to witness trends such as ***label-free detection****, drug discovery out-sourcing, 3D culture and stem cells*

Cell-based Assays Market by Product, Application, End-user, Markets & Markets, 2014

KEY MARKET TRENDS

- Rising incidence of cancer and neuro-degenerative diseases propel the cell analysis market
- Advancements in biotechnology, optics, electronics and image analysis continue to create market opportunities
- Need for standardization and maintaining cell viability/optimal environment drive automation of cell culture systems
- Integration of microfluidics and nanobio-technology with microscopy imaging platforms enables scientists to conduct more biologically relevant investigations, unattainable with conventional techniques
- Increased use of 3D cell culture methods drives the need for new analytical imaging technologies

Present and future cell culturing. Lab-on-a-chip technology allows cells to be cultured in a micro-environment.

TARGET CUSTOMERS

Academic Research

- Every academic lab involved in cell based preclinical research

Pharmaceutical

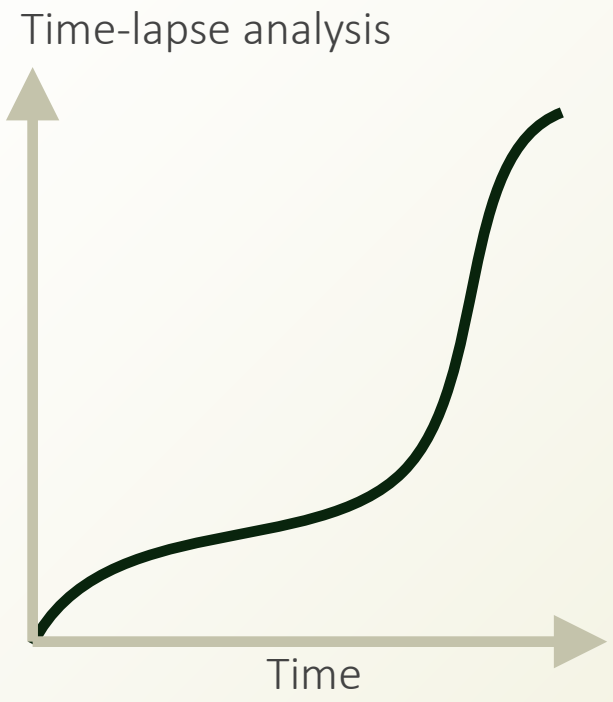
- Mechanism of action studies
- Secondary screening
- Toxicology
- Bio-production

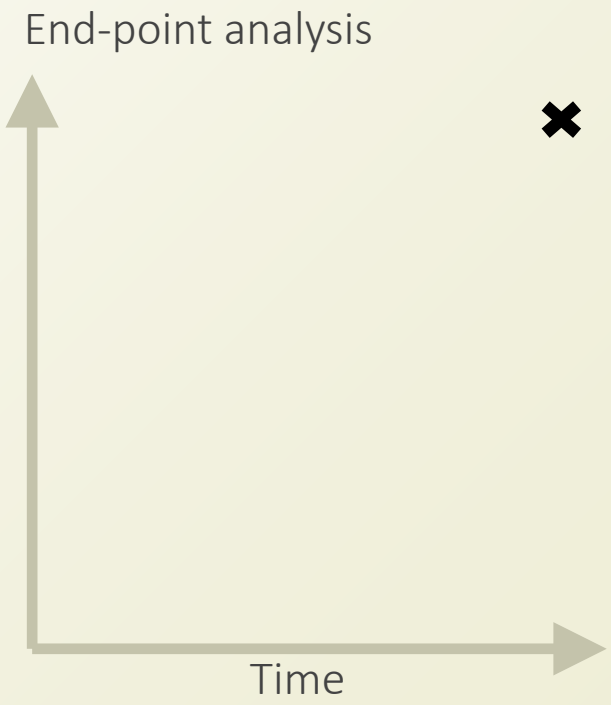
Biotechnology

- Every company attempting to automate cell culturing process
- Every company performing cell-culture experiments (including household, cosmetics, tobacco, etc.)

END-POINT VS. TIME-LAPSE CELL ANALYSIS

- Fixed cell analysis and the limitations of labeled live cell analysis has led to that most cell culture based experiments are only analyzed at the end of the experiment – *end-point cell analysis*
- Label-free live cell analysis allows cell culture based experiments to be continuously monitored and analyzed through out the experiment – *time-lapse cell analysis*





MARKET OPPORTUNITY

Transition from end-point to time-lapse cell analysis

Time-lapse microscopy allows cell based preclinical research to transition from end-point to time-lapse cell analysis

End-point cell analysis

- Single observation at the end of the experiment
- One cell culture → one data point
- Analysis of dead cells

Time-lapse cell analysis

- Multiple observations during the experiment
- One cell culture → multiple data points
- Analysis of living cells

Time-lapse of a dividing cell

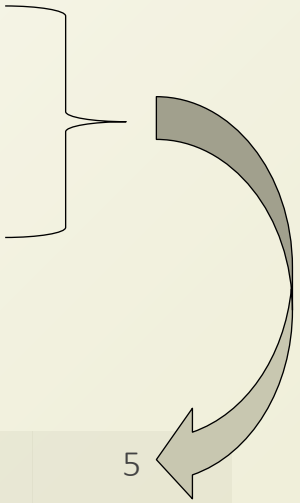
> *Quantifying over time is crucial for a full understanding of cell systems. I am convinced that time-lapse microscopy will enable the next level of insight*

Prof. Timm Schroeder, ETH Zurich

TIME-LAPSE MICROSCOPY

- Modern computer technology makes it in principle very easy to record time-lapse microscopy movies of living cells
- However, the nature of cells and limitations of conventional microscopes make time-lapse recording and analysis challenging in practice

1. Cultured cells quickly die outside an incubator environment
2. To keep the cells in focus some type of autofocus is needed
3. Toxic stains are needed to automatically track cells
4. Cytometric software is needed to process the huge amount of data in time-lapse movies
5. Toxic stains are needed to quantitatively observe molecular specificity



		Addressed issues				
Microscope type	Cost (K USD)	1	2	3	4	5
Conventional	+10					
Low-end time-lapse	~10	√				
High-end time-lapse	+100	√	√			
Phase Holographic Imaging	**20 -**	**√**	**√**	**√**	**√**	**√**

HOLOMONITOR M4

Label-free live cell analysis

- Addresses issues 1-4
- Over 40 units in operation with customers and key opinion leaders
  - Harvard and Northeastern University, Boston
  - University of California, San Francisco
  - Israel Institute for Biological Research
  - For additional users see www.phiab.se/publications/users
- After customer feedback several pilot builds have been manufactured
- Production will move into series production in Q3 2015
- For additional product information see www.phiab.se/products/products

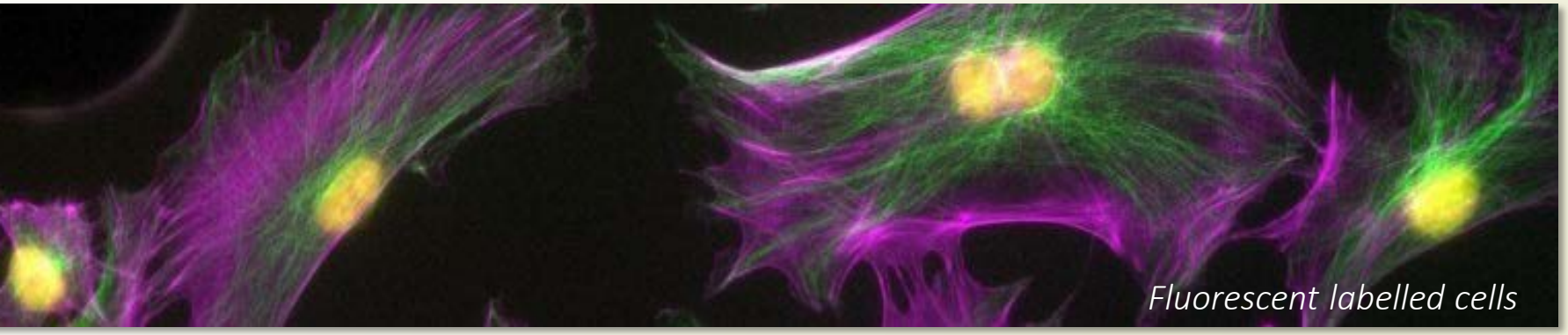
"The HoloMonitor platform offers unique 4-dimensional imaging capabilities that greatly enhance our understanding of both functions, which was previously unachievable by other technologies

Ed Luther, Northeastern University, Boston

HOLOMONITOR M5

Minimally invasive live cell analysis

- Addresses issues 1-5
- Cell biologists use fluorescent labels to identify biochemical compounds
- Fluorescent labels are activated by light of a specific wavelength. These labels are toxic, especially when activated
- By combining HoloMonitor technology with fluorescence detection capabilities, the activation of fluorescent labels can be dramatically reduced to minimize the toxic effect on cell behavior
- HoloMonitor M5 is being developed in collaboration with Lund University. Funding is provided by the Swedish Research Council (Vetenskapsrådet)
- HoloMonitor M4 + fluorescent capability = HoloMonitor M5



Fluorescent labelled cells

COMPETITION

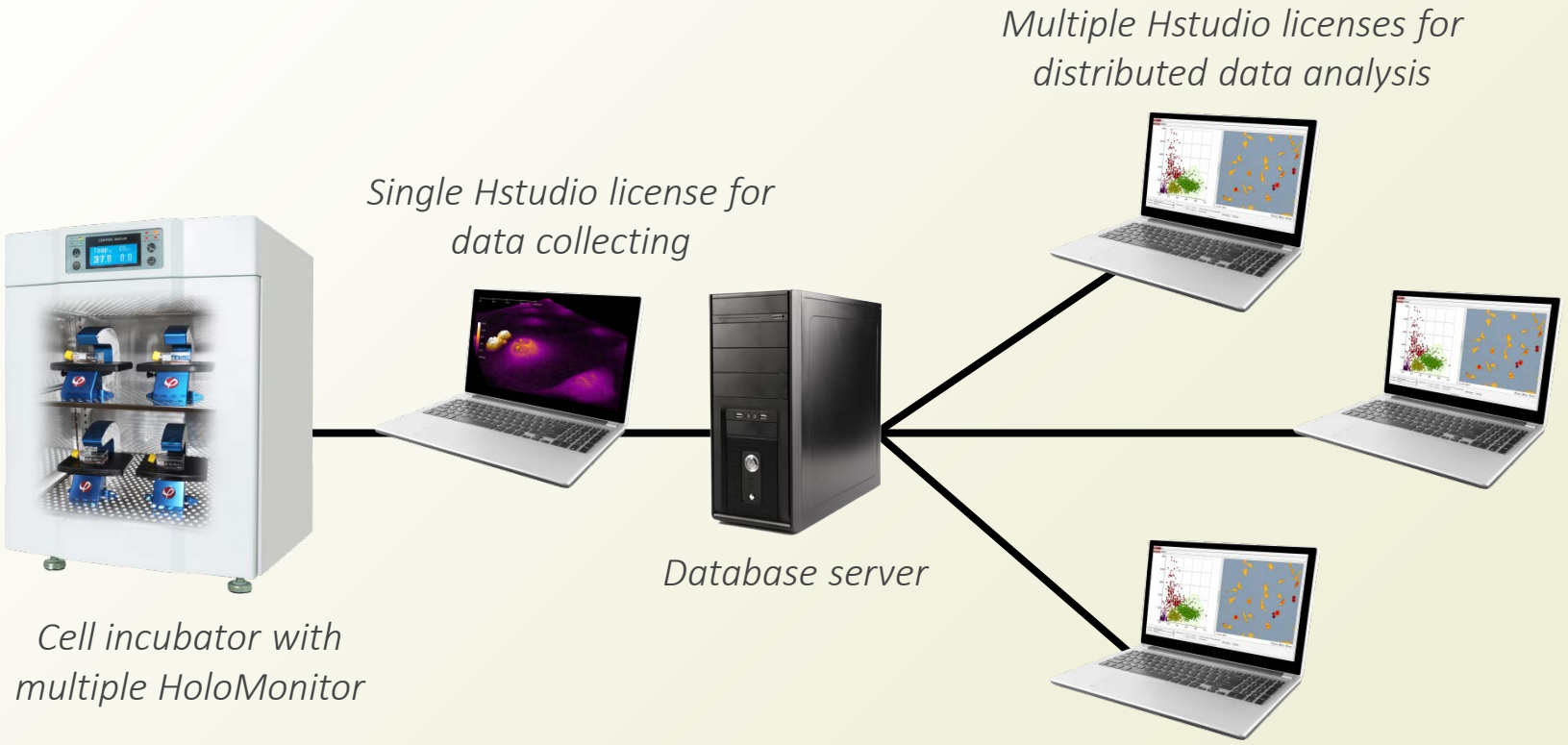
		Addressed issues				
Microscope type	Cost (K USD)	1: Incubator environment	2: Autofocus	3: No toxic stains needed to track cells	4: Cytometric software	5: No toxic stains needed to observe molecular specificity
Conventional	+10					
Low-end time-lapse	~10	√				
High-end time-lapse	+100	√	√			
Competing holographic	~50 -100		√	√		
HoloMonitor M4	**20-35**	**√**	**√**	**√**	**√**	
HoloMonitor M5		**√**	**√**	**√**	**√**	**√**

Microscope type	Suppliers
Conventional	Nikon, Olympus, Zeiss
Low-end time-lapse	Small technology companies (NanoEntek, Etaluma, CytoMate)
High-end time-lapse	Nikon, Olympus, Zeiss, Thermo Fisher, GE Healthcare
Competing holographic	Small technology companies (Ovizio, Lynceé Tec, NanoLive)

HSTUDIO

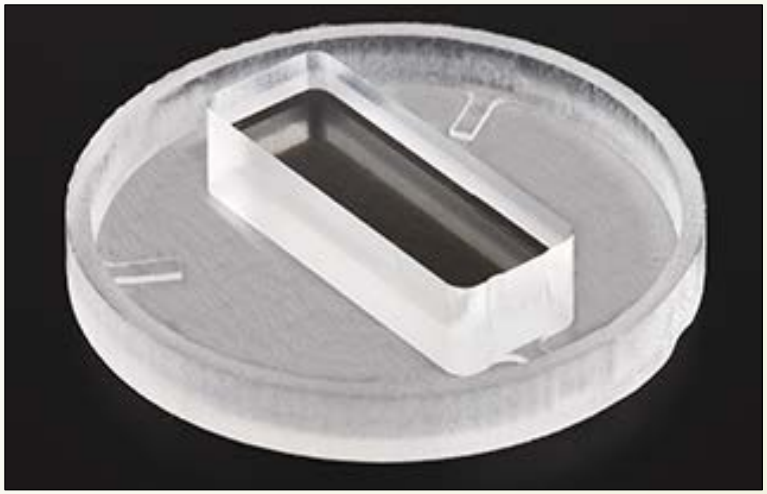
Proprietary cell analysis software

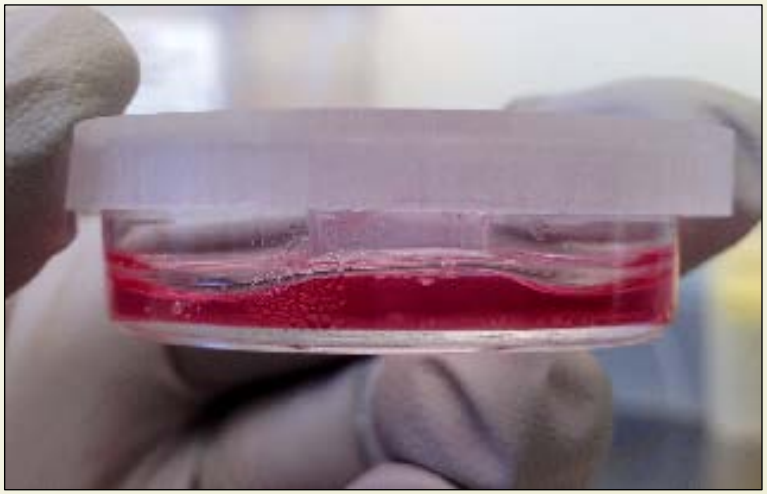
- Dedicated cell analysis software is a key competitive advantage
- Current version is stable and very appreciated by customers. Few issues have been reported by customers
- Development focus on facilitating distributed data analysis to provide additional revenue source



CONSUMABLES PIPELINE

- To take full advantage of time-lapse cell analysis a new generation of cell culture vessels is needed
- Conventional cell culture vessels are designed for end-point cell analysis
- PHI is currently developing a new generation of cell culture vessels and other consumables
- Key to the long term profitability
- Makes HoloMonitor technology more convenient to use





The PHI petri dish lid eliminates disturbances from condensation droplets and surface vibrations

INTELLECTUAL PROPERTY

- 2 registered trademarks, HoloMonitor and HoloMetrics
- 6 patent families
- 12 granted patents

METHOD AND APPARATUS FOR HOLOGRAPHIC REFRACTOMETRY

Patent	Country	Expiry date
4 739 214	Japan	2024-Oct-07
1 676 121	Denmark	2024-Oct-07
1 676 121	France	2024-Oct-07
60 2004 030 928.1	Germany	2024-Oct-07
1 676 121	The Netherlands	2024-Oct-07
1 676 121	Sweden	2024-Oct-07
1 676 121	Switzerland-Liechtenstein	2024-Oct-07
1 676 121	UK	2024-Oct-07

METHOD AND APPARATUS FOR ANALYSIS OF A SAMPLE OF CELLS

Patent	Country	Expiry date
ZL200680048900.7	China	2026-Dec-22
5 182 945	Japan	2026-Dec-22
7 948 632	USA	2027-Sep-30

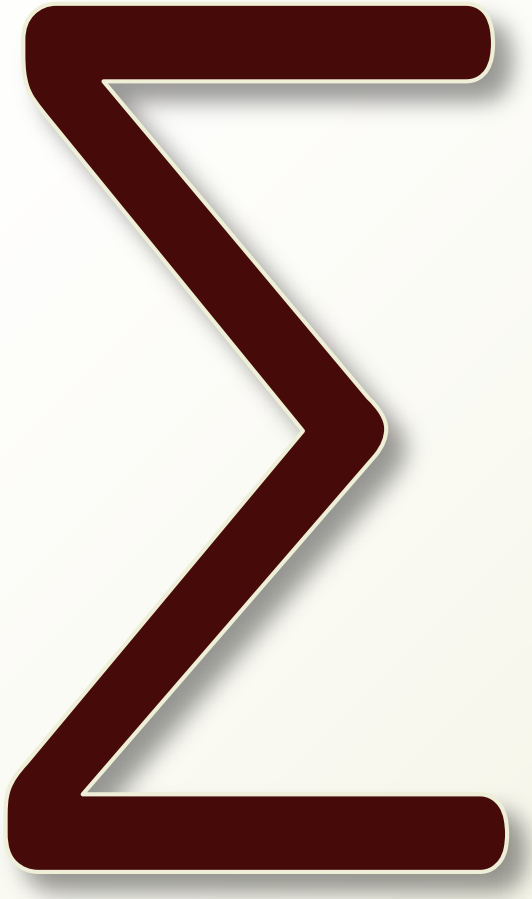
METHOD FOR AND USE OF DIGITAL HOLOGRAPHIC MICROSCOPY AND IMAGING ON LABELLED CELL SAMPLES

Patent	Country	Expiry date
8 937 756	USA	2030-Feb-09

EXIT STRATEGY

- Establish HoloMonitor technology through
  - initial sales in key markets: US, Germany, Switzerland, UK, Japan and China
  - collaborations with key opinion leaders
- Expand use of technology through Centers of Excellence in life science hotspots
  - Boston, San Diego, San Francisco
  - London, Basel, Heidelberg
  - Tokyo
- To create visibility in the US, establish direct PHI presence in the Boston area
- Complete development of HoloMonitor M5 and consumables pipeline
- Seek global distribution through major life science tools companies
- Divest business when substantial market traction has been achieved

SUMMARY



- PHI's technology allows cell based preclinical research to transition from end-point to time-lapse cell analysis
- The global market is estimated to be valued at $8.7 billion USD
- Company sales in 2014/15: 2.7 (1.4) MSEK
- Over 40 units in operation at customers and key opinion leaders
- Production moves into series production in Q3 2015
- Exit strategy
  - increase sales,
  - expand strategic marketing and
  - divest the business

Holographic Imaging

Phase

Time-lapse cytometry for biologists, by biologists

Thank You

www.phiab.se