



## Corporate Presentation

July 2013

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# Forward Looking Statements

This presentation includes statements that are, or may be deemed, “forward-looking statements.” In some cases, these forward-looking statements can be identified by the use of forward-looking terminology, including the terms “believes,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should,” “approximately” or, in each case, their negative or other variations thereon or comparable terminology, although not all forward-looking statements contain these words. They appear in a number of places throughout this presentation and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned discovery and development of drugs targeting cancer stem cells, the strength and breadth of our intellectual property, our ongoing and planned preclinical studies and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, the degree of clinical utility of our products, particularly in specific patient populations, expectations regarding clinical trial data, our results of operations, financial condition, liquidity, prospects, growth and strategies, the length of time that we will be able to continue to fund our operating expenses and capital expenditures, our expected financing needs and sources of financing, the industry in which we operate and the trends that may affect the industry or us.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this presentation as a result of, among other factors, the factors referenced in the “Risk Factors” section of our Registration Statement on Form S-1 initially filed with the Securities and Exchange Commission on May 6, 2013 as subsequently amended to date (our “Registration Statement”). In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this presentation, they may not be predictive of results or developments in future periods. Any forward-looking statements that we make in this presentation speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this presentation, except as required by law.

You should read carefully our “Special Cautionary Notice Regarding Forward-Looking Statements” and the factors described in the “Risk Factors”

sections of our Registration Statement to better understand the risks and uncertainties inherent in our business.



# Free Writing Prospectus Statement

This presentation highlights basic information about us and the offering. Because it is a summary, it does not contain all of the information that you should consider before investing.

We have filed a registration statement (including a preliminary prospectus) with the SEC for the offering to which this presentation relates. The registration statement has not yet become effective. Before you invest, you should read the preliminary prospectus in the registration statement (including the risk factors described therein) and other documents we have filed with the SEC for more complete information about us and the offering.

You may get these documents for free by visiting EDGAR on the SEC Web site at <http://www.sec.gov>. The preliminary prospectus, dated June 21, 2013, is available on the SEC Web site at <http://www.sec.gov>. Alternatively, we or any underwriter participating in the offering will arrange to send you the prospectus if you contact Aegis Capital Corp., Prospectus Department, 810 Seventh Avenue, 18th Floor, New York, NY 10019, telephone: 212-813-1010, e-mail: [prospectus@aegiscap.com](mailto:prospectus@aegiscap.com)



# Offering Summary

## Deal Terms

SHARES OFFERED	1,650,000 (100% Primary)
PRICE RANGE	\$10.00 - \$12.00 per Share
EXCHANGE / TICKER	NASDAQ Capital Market / HTBX
OVER-ALLOTMENT	15% or 247,500 (100% Primary)
USE OF PROCEEDS	Clinical Development of HS-110 and HS-410 and Other General Corporate Purposes
SOLE BOOK-RUNNER	Aegis Capital Corp
CO-MANAGER	Cantor Fitzgerald & Co.



# The Heat Biologics Team

## **Jeffrey Wolf**

*Founder, Chairman and CEO*

- Founded Heat Biologics and advanced company to current clinical stage
- Founder/CEO of several biotech companies including Elusys Therapeutics (founder/Chairman/CEO) TyRx Pharma (co-founder/Chairman), Avigen (NASDAQ: AVGN) (co-founder/director)
- BA, University of Chicago; JD, New York University School of Law; MBA, Stanford Business School

## **Sandra Silberman, MD, PhD**

*Medical Officer*

- Oversaw the clinical development of Tarceva™ at Pfizer
- Led global development and FDA approval of Gleevec™ at Novartis. Senior oncology clinical development positions Eisai and Quintiles
- MD, Cornell University Medical College; Ph.D. in Tumor Immunology, Johns Hopkins University

## **Matt Czajkowski**

*Chief Financial Officer*

- Chief Financial Officer at Pozen Pharmaceuticals (NASDAQ: POZN)
- BA, Harvard College; MBA, Harvard Business School

## **Jennifer Harris, Pharm. D.**

*VP of Clinical and Regulatory Affairs*

- Significant experience in the clinical development of cancer immunotherapies with Dendreon, Celgene and Novaquest (Quintiles)
- BS and Pharm.D, University of North Carolina, Chapel Hill

## Scientific Advisory Board

### **Eckhard Podack, MD, Ph.D.**

*Chairman of Scientific Advisory Board  
Chairman of Microbiology and Immunology,  
University of Miami*

### **James Allison, Ph.D.**

*Former Chairman of Immunology Program,  
Memorial Sloan Kettering*

### **Sol Barer, Ph.D.**

*Co-founder, former Chairman and CEO, Celgene*

### **John Nemunaitis, M.D.**

*Executive Medical Director,  
Mary Crowley Cancer Research Center*

### **Justin Stebbing, M.D., Ph.D.**

*Imperial College, London*

### **Daniel Von Hoff, M.D.**

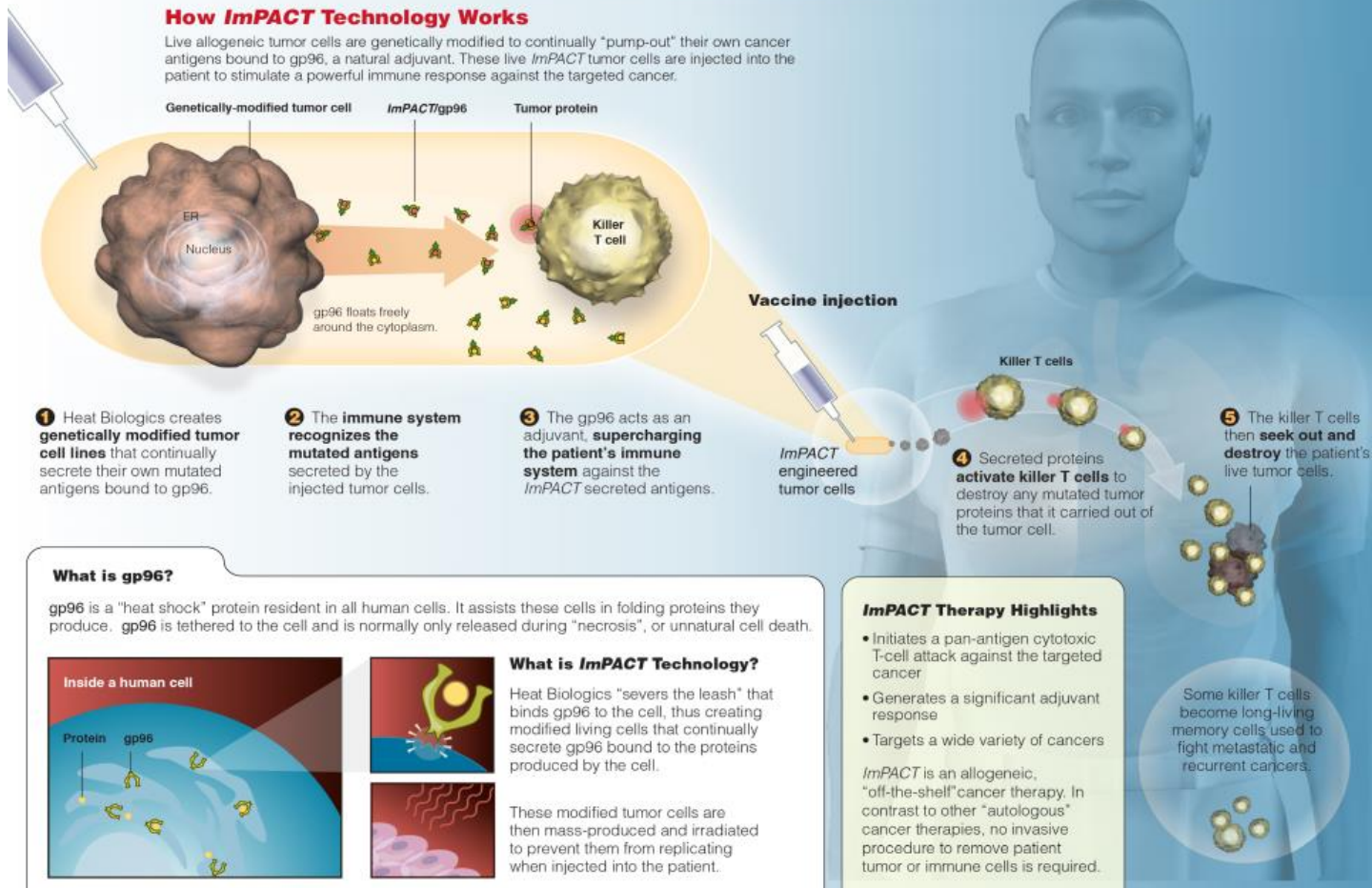
*Translational Genomics Research Institute  
Past President of American Association of  
Cancer Research*



Heat Biologics' proprietary **Immune Pan Antigen Cytotoxic Therapy (ImPACT)** reprograms live "allogeneic" cancer cells to continually secrete their own antigens bound to heat shock protein gp96 to seek out and destroy a variety of tumors.

### How ImPACT Technology Works

Live allogeneic tumor cells are genetically modified to continually "pump-out" their own cancer antigens bound to gp96, a natural adjuvant. These live ImPACT tumor cells are injected into the patient to stimulate a powerful immune response against the targeted cancer.



**1** Heat Biologics creates **genetically modified tumor cell lines** that continually secrete their own mutated antigens bound to gp96.

**2** The **immune system recognizes the mutated antigens** secreted by the injected tumor cells.

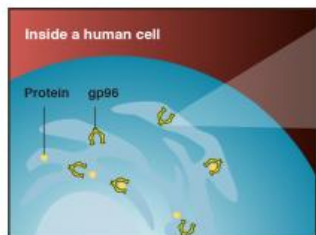
**3** The gp96 acts as an adjuvant, **supercharging the patient's immune system** against the ImPACT secreted antigens.

**4** Secreted proteins **activate killer T cells** to destroy any mutated tumor proteins that it carried out of the tumor cell.

**5** The killer T cells then **seek out and destroy** the patient's live tumor cells.

#### What is gp96?

gp96 is a "heat shock" protein resident in all human cells. It assists these cells in folding proteins they produce. gp96 is tethered to the cell and is normally only released during "necrosis", or unnatural cell death.



#### What is ImPACT Technology?

Heat Biologics "severs the leash" that binds gp96 to the cell, thus creating modified living cells that continually secrete gp96 bound to the proteins produced by the cell.

These modified tumor cells are then mass-produced and irradiated to prevent them from replicating when injected into the patient.

#### ImPACT Therapy Highlights

- Initiates a pan-antigen cytotoxic T-cell attack against the targeted cancer.
- Generates a significant adjuvant response
- Targets a wide variety of cancers

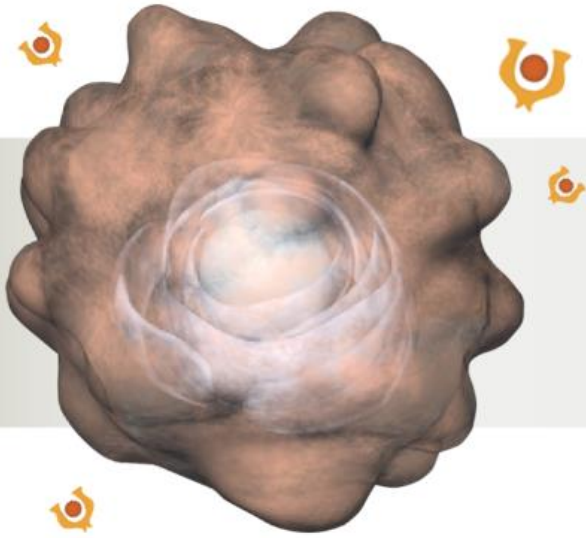
ImPACT is an allogeneic, "off-the-shelf" cancer therapy. In contrast to other "autologous" cancer therapies, no invasive procedure to remove patient tumor or immune cells is required.

Some killer T cells become long-living memory cells used to fight metastatic and recurrent cancers.

# Heat Biologics Highlights

<b>Broad-based Immunotherapy Platform</b>	<ul style="list-style-type: none"> <li>• Transformative immunotherapy platform that unleashes a robust pan-antigen T-cell attack against a wide range of cancers</li> <li>• Fully-allogeneic, “off-the-shelf” drugs with COGS &lt; 5% of autologous cancer vaccine approaches</li> <li>• Multiple near-term registration opportunities (&gt;\$60 Billion TAM)</li> </ul>
<b>Promising Clinical Data</b>	<ul style="list-style-type: none"> <li>• 18-patient Phase 1 investigator-sponsored IND in advanced non-small cell lung cancer             <ul style="list-style-type: none"> <li>– Positive safety data with no treatment-related SAEs</li> <li>– Powerful disease-specific immune activation</li> <li>– Preliminary evidence that immune activation corresponds with increased overall survival</li> </ul> </li> <li>• Median 1-year overall survival rate in advanced NSCLC of 43% compared favorably to a 5.5% rate based on published data from a 43-patient advanced NSCLC population</li> <li>• One patient survives &gt;3 yrs. and another patient survives &gt;4 yrs. since starting therapy</li> </ul>
<b>Diverse Clinical Pipeline</b>	<ul style="list-style-type: none"> <li>• IPO net proceeds will be used to progress two drug candidates through Phase 2 clinical trials             <ul style="list-style-type: none"> <li>– HS-110 for non-small cell lung cancer (NSCLC)</li> <li>– HS-410 for bladder cancer</li> </ul> </li> </ul>
<b>Milestones</b>	<ul style="list-style-type: none"> <li>• IPO net proceeds expected to progress <u>two</u> clinical programs through Phase 2 trials</li> <li>• Multiple value-creating milestones planned over the next 12-24 months</li> </ul>
<b>Experienced Team</b>	<ul style="list-style-type: none"> <li>• Strong management and scientific team includes SAB members Sol Barer (Celgene), James Allison (Sloan Kettering), Eckhard Podack (Miami), Daniel Von Hoff (TGen)</li> </ul>






## Heat's *ImPACT* Therapy

### Living Drug Factories

Antigen and adjuvant delivery in a single package







Dr. Eckhard Podack transforms living cancer cells into **factories** that secrete a wide variety of antigens to our immune system

- Chairman, Dept. of Immunology University of Miami
- Discover of Perforin
- Inventor of Seattle Genetics CD30 antibody (Adcetris®) recently approved by FDA for Hodgkin Lymphoma
- Inventor of Heat's **ImPACT** Technology



Cutting Edge: Tumor Secreted Heat Shock-Fusion Protein Elicits CD8 Cells for Rejection.  
*K. Yamazaki, T. Nguyen, E.R. Podack.*

Molecular and Cellular Requirements for Enhanced Antigen Cross-Presentation to CD8 Cytotoxic T Lymphocytes.  
*S. Oizumi, N. Strbo, S. Pahwa, V. Deyev, E.R. Podack.*

Surmounting tumor-induced immune suppression by frequent vaccination or immunization in the absence of B cells.  
*S. Oizumi, V. Deyev, K. Yamazaki, T. Schreiber, N. Strbo, J. Rosenblatt, E.R. Podack.*

Gp96<sup>SIV</sup> Ig immunization induces potent polypeptide specific, multifunctional memory responses in rectal and vaginal mucosa.  
*N. Strbo, M. Vaccaric, S. Pahwa, M.A. Kolherb, E. Fishera, J. Gonzalez, M.N.*



Tumor-induced suppression of CTL expansion and subjugation by gp96-Ig vaccination.  
*T.H. Schreiber, V. Deyev, J.D. Rosenblatt, E.R. Podack.*

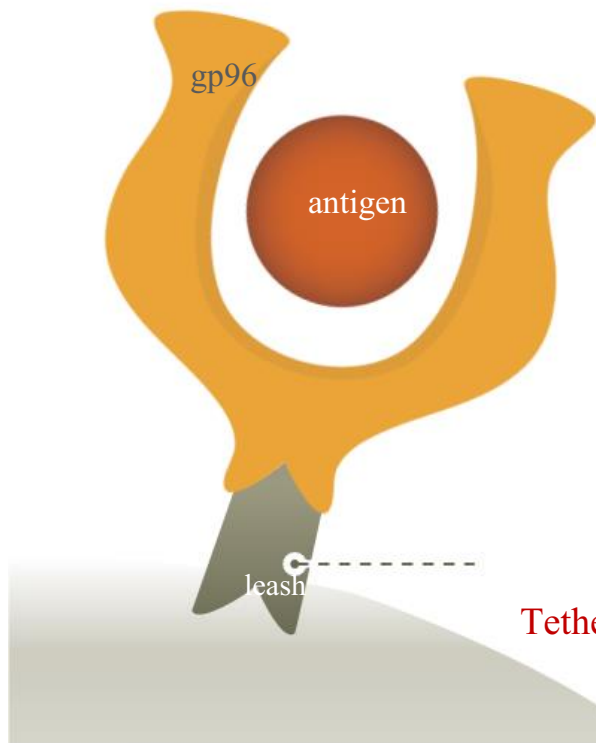
Cell surface expression of heat shock protein gp96 enhances cross-presentation of cellular antigens and the generation of tumor-specific T-cell memory.  
*L. Dai, B. Liu, M.M. Caudill, H. Zheng, Y. Qiao,*



Cell-secreted gp96-Ig-peptide complexes induce lamina propria and intraepithelial CD8+ cytotoxic T lymphocytes in the intestinal mucosa.  
*M. Srinivasan, S. Oizumi, V. Deyev, J.D. Rosenblatt, E.R. Podack.*



# Introducing gp96 — *Immune System's "Swiss Army Knife"*\*



## “Molecular Warning System”

- “Chaperone” protein expressed in all our cells and variety of tumors
- Activates a pan-antigen T-cell response by enabling MHC I antigen cross-presentation to CD8+ T-cells
- Gp96 + client protein naturally released via necrosis
- Among the most powerful adjuvants and the only adjuvant to show exclusive specificity to CD8+ T-cells
  - Provides non-specific signals to the innate immune system and specific signals to adoptive immune system

Tethered to our cells with a leash

\* Schild, H. & Rammensee, H. *Gp-96 - The Immune System's Swiss Army Knife*, Nature Immunology 2, 100-101 (2000)

Heat Biologics

## *ImPACT* Therapy — “Severing the Leash”

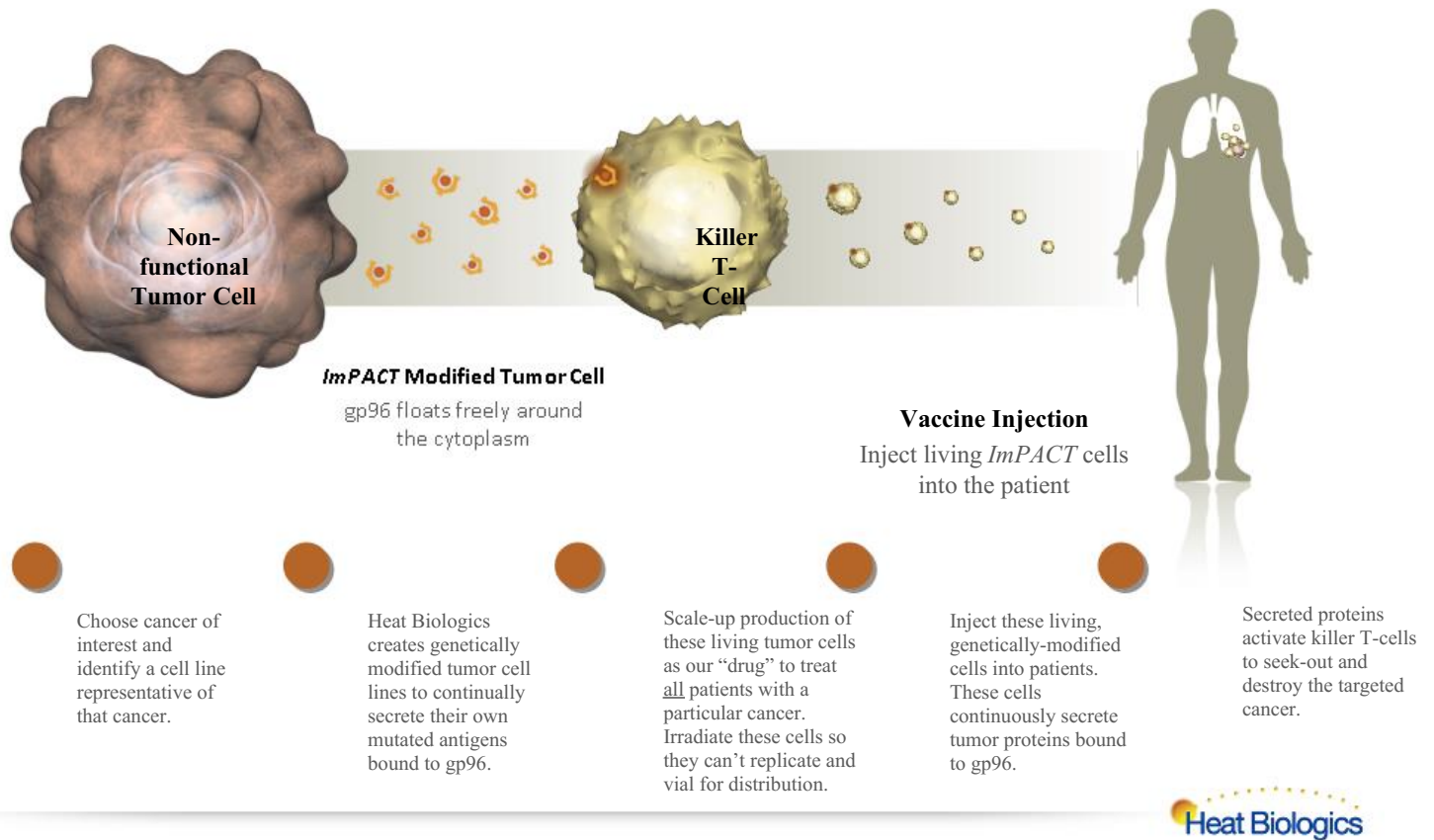


- Genetically modify tumor cells by “severing the leash” that binds the gp96 to the cell
  - Enables living cancer cells to “pump-out” their own antigens along with their gp96 chaperone
- Mimics necrotic cell death to activate powerful pan-antigen cytotoxic T-cell immune response
- Natural biological process to deliver antigens and adjuvant to our immune system
- “Off-the-shelf” therapy designed to enable a fully in vivo attack against a wide variety of cancers

Heat Biologics *ImPACT* technology removes the leash that binds gp96 to the cell, creating cells that continually secrete gp96

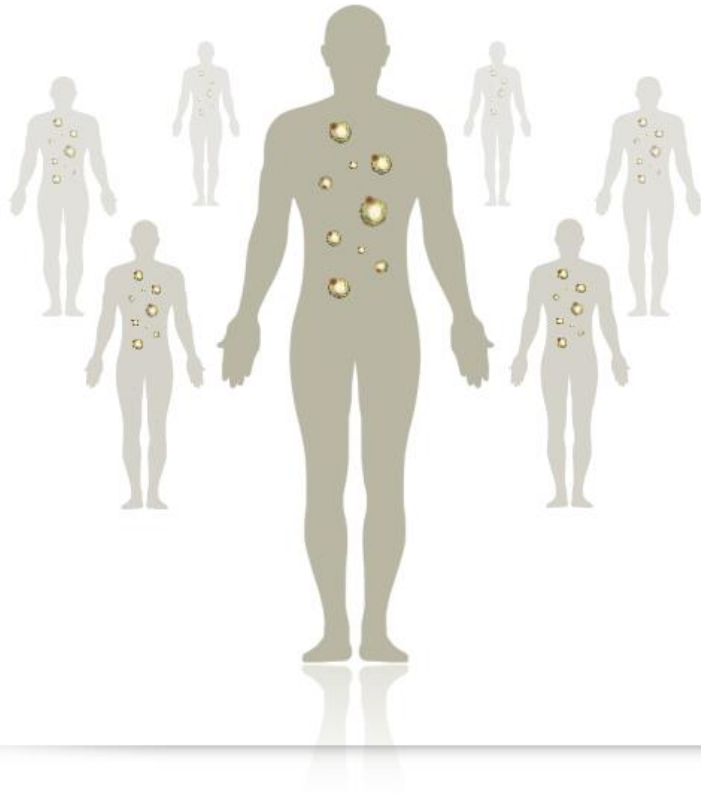


# ImPACT Therapy — Process



# Fully-Allogeneic Approach

## An Off-the Shelf Therapy



### Approach

- Allogeneic, “off-the-shelf” treatment created from a master cell line
- No tumor cells, blood or anything else extracted from the patient
- Non-invasive

### Benefits

- Unlimited drug supply enables immediate treatment and frequent administration with no patient-specific processing
- Pan-antigen immune response
- Less expensive to produce and administer than autologous therapies with COGS < 5% of autologous approaches with fewer logistical hurdles



# Strong Intellectual Property Protection

## IP Estate with Broad and Early Filings

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### *ImPACT* Platform Technology

- US and foreign patents issued for *ImPACT* technology for the treatment of cancer and viral disease
  - Additional patents on proprietary cell lines and clinical data
- 

### Worldwide Filings

- 5 patent families representing over 50 patent applications
- Enforceable patents issued in 15 countries and counting



# Lung Cancer and HS-110

## Background

Lung Cancer is the Second Most Common Cancer in US with No Reliable Treatment Options for Late-Stage Patients

**“Without any chemotherapy, the average person will live about 4½ months.**  
With chemotherapy most will live longer and some will live a shorter time. More recent chemotherapy trials have shown that people live about 3 months longer than if they did not get chemotherapy...  
**... Even with chemotherapy, the chance of being alive at one year is about 30-50%;**  
the chance of dying within this year is 50-70%.”

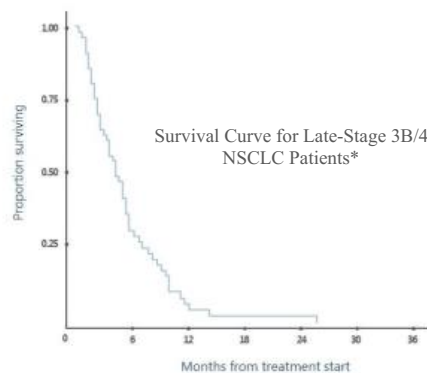
— American Society for Clinical Oncology (ASCO) Guidelines

## Current Treatment

- Surgical Resection
- Radiation Therapy
- Chemotherapy
  - 3-6 cycles
  - Each cycle lasts 3-4 weeks
- Targeted Therapies

## Survival Prospects

- Median survival ~ 4.5 months\*
- 1 year survival >6%\*



\* Massarelli E. Lung Cancer;2003;39 - Meta Analysis

## Heat's HS-110 Therapy

- Cells are genetically modified to secrete gp96 and most known (and many unknown) lung cancer antigens
- Pan-antigen cytotoxic T-cell immune response

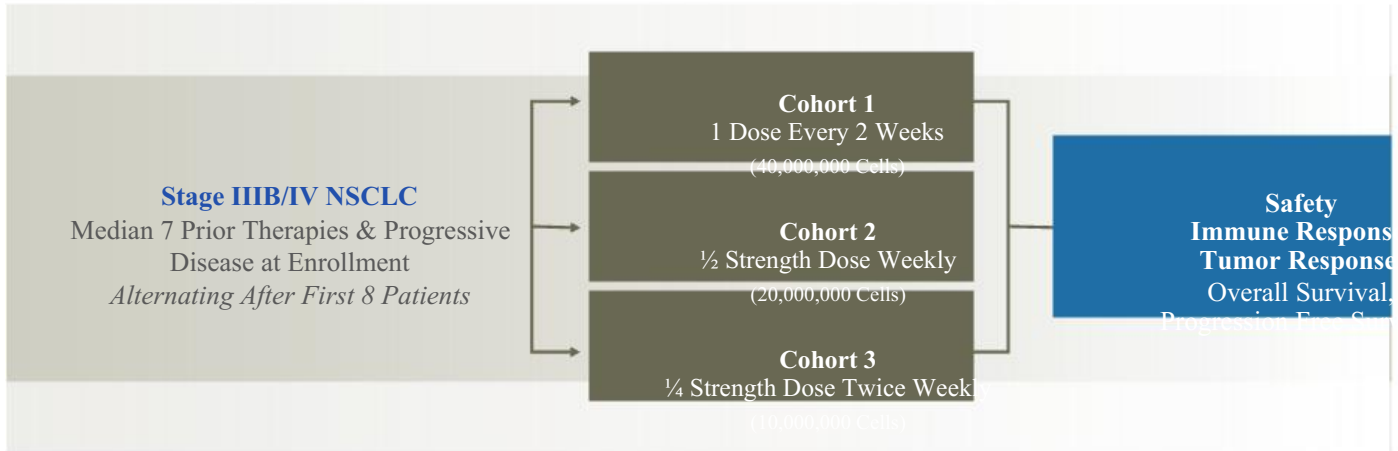
## Treatment

- Powerful immune activation
- Positive safety profile based on preclinical studies and one clinical study
- The drug is administered in a simple, once-a-week injection





# HS-110: Phase 1 Lung Cancer Trial Design



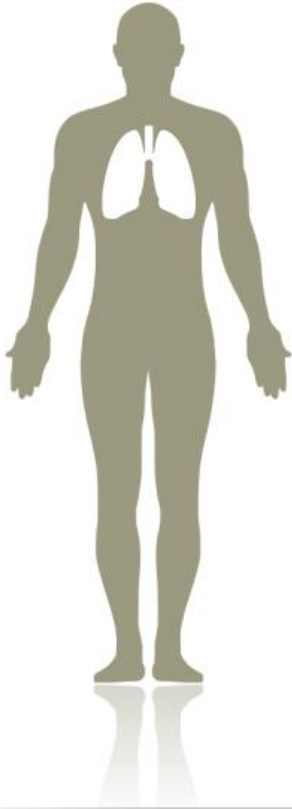
- NIH-funded, open-label, single center investigator-sponsored IND
- 18 patients with late-stage NSCLC
- Participants had previously failed multiple lines of therapy







# HS-110 NSCLC Phase 1 Clinical Trail Results



- **Well-tolerated** with no overt toxicity and no treatment-related SAEs
- 18 patients treated, 15 patients completed first course of therapy, 2 patients completed 3 courses of therapy
- **Single agent clinical activity** in late-stage 3b and 4 lung cancer
  - As is typical in immunotherapy, no observed partial or complete responses
  - 7 patients exhibited stable disease after single course of therapy
- **Immune response observed** in 73% (11 out of 15) of patients who completed their first course of therapy
  - **Immune response predictive of survival** (HR: 0.021, 95% CI:0.002-0.204)
    - The 11 immune responders exhibited a median survival of 16.9 months (95% CI: 7.1-20) while the 4 immune non-responders exhibited a median survival of 4.5 months, which is consistent with the expected survival times in this patient population
  - **Two late-stage patients survive >3 years**
    - One HS-110 patient alive >3 yrs. and another patient still alive >4 yrs.
- **Median 1 year overall survival rate** of patients in the study was 44% (95% CI: 21.6-65.1) comparing favorably to a 5.5% rate based on published data from a 43-patient advanced NSCLC population





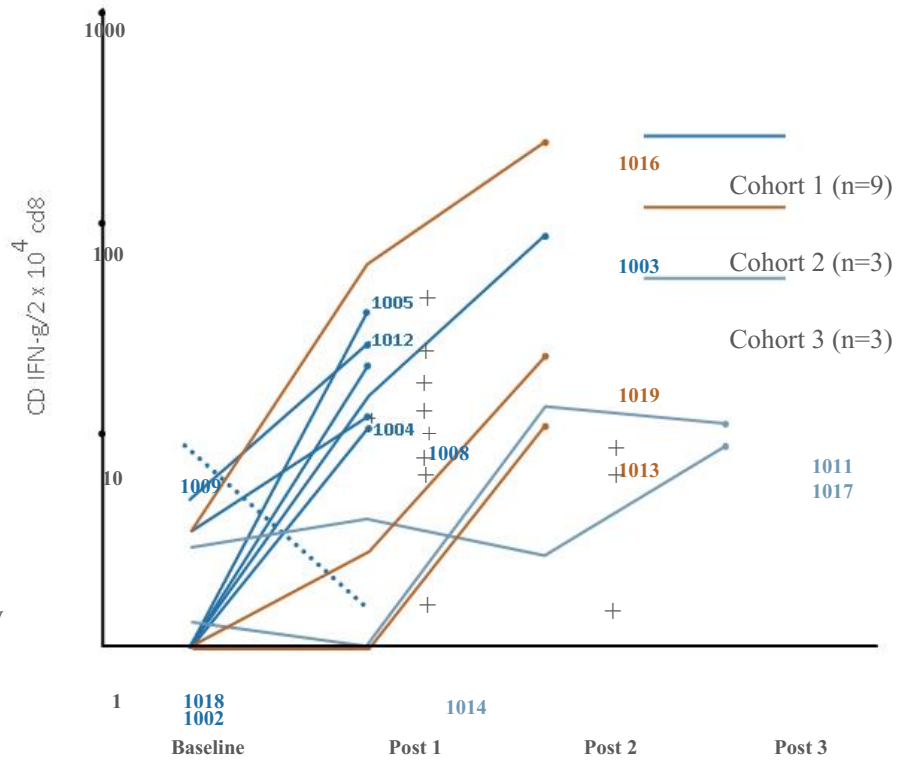
# Highly Activated Immune Response

## Methodology

- Samples collected for immune response at baseline and after a minimum of one 6-week course of therapy were analyzed
- To determine the frequency of CD8 IFN- $\gamma$ , purified CD8 T cells collected from patients were stimulated with vaccine
- + Indicates first increase, solid lines indicate immune response (IR+), dashed lines no response (IR-)

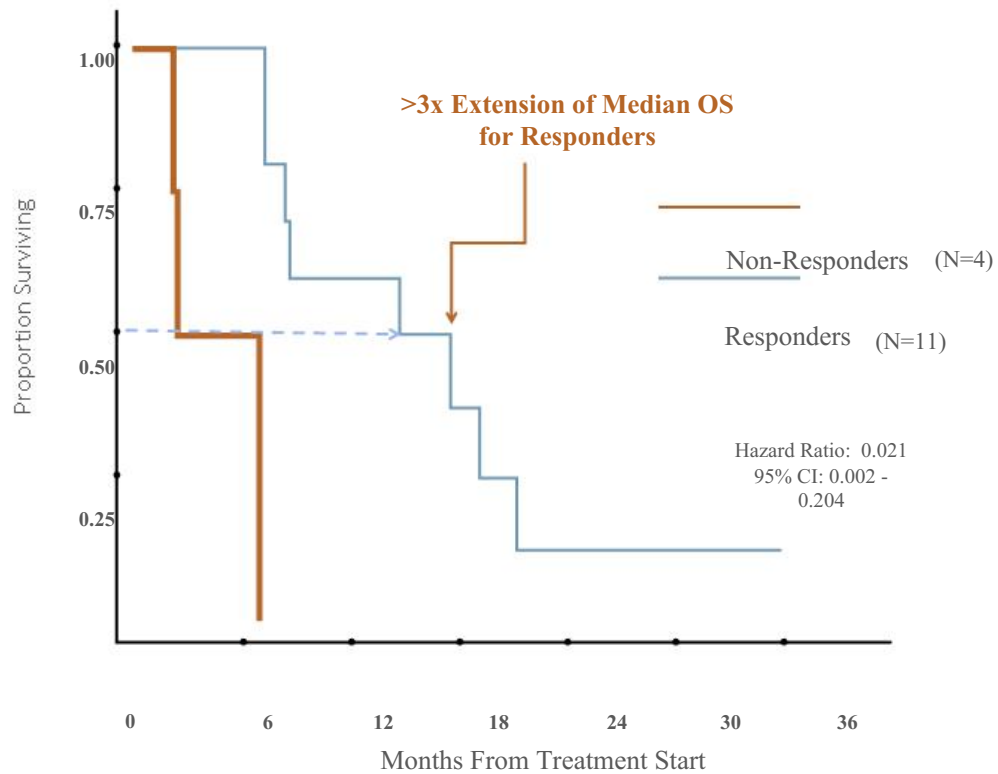
## Results

- In 11 of the 15 patients (73%) completing the first course of therapy with HS-110, there was a twofold or greater increase in CD8 cells secreting interferon gamma (CD8-CTL IFN- $\gamma$ ) following vaccination





# Immune Response Predictive of Survival

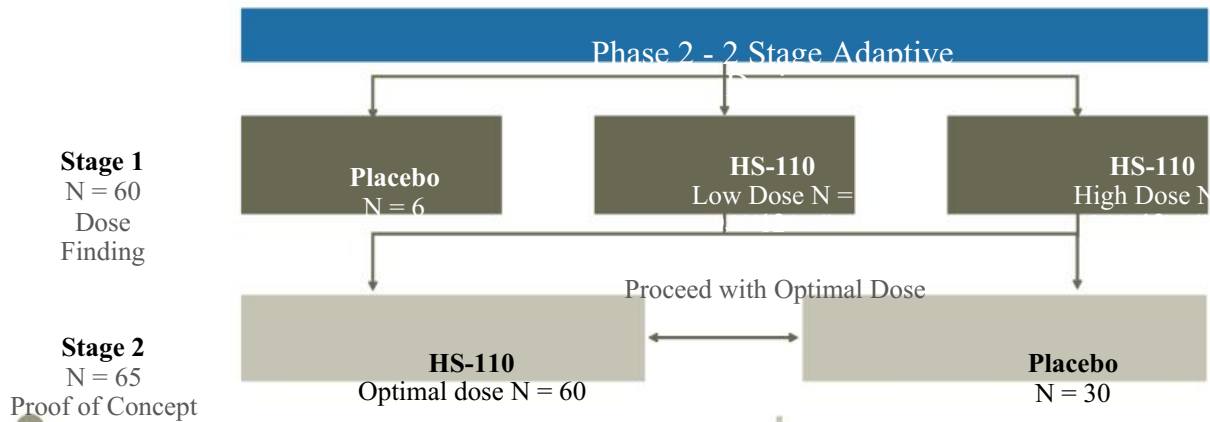


In 11 of the 15 patients (73%) completing the first course of therapy with HS-110, there was a twofold or greater increase in CD8 cells secreting interferon gamma (CD8-CTL IFN- $\gamma$ ) following vaccination. In a non-prespecified analysis, the responders had a significant increase in median overall survival compared to non-responders in the trial, from 4.5 months to 16.9 months





# Phase 2 NSCLC Trial Design



## Inclusion Criteria

- Stage III/IV NSCLC patients
- Prior treatment with platinum doublet, crizotinib, erlotinib as 1st line treatment
- Achieved clinical response (CR/PR) or disease stabilization following 1st line treatment

## Trial Objectives

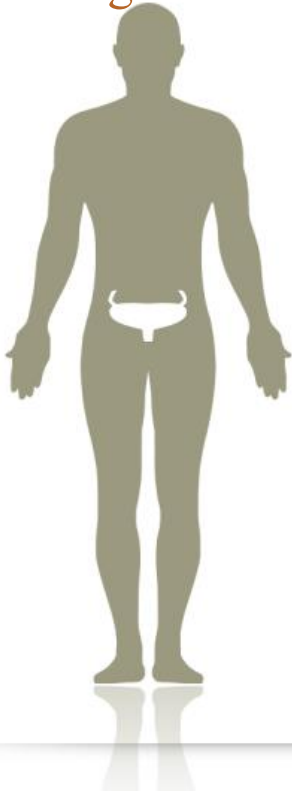
- Stage 1: Dose finding and safety
- Stage 2: Progression-free survival



In addition, a grant-funded, investigator-sponsored Phase 1 NSCLC trial will explore use of HS-110 as a combination therapy



## Background



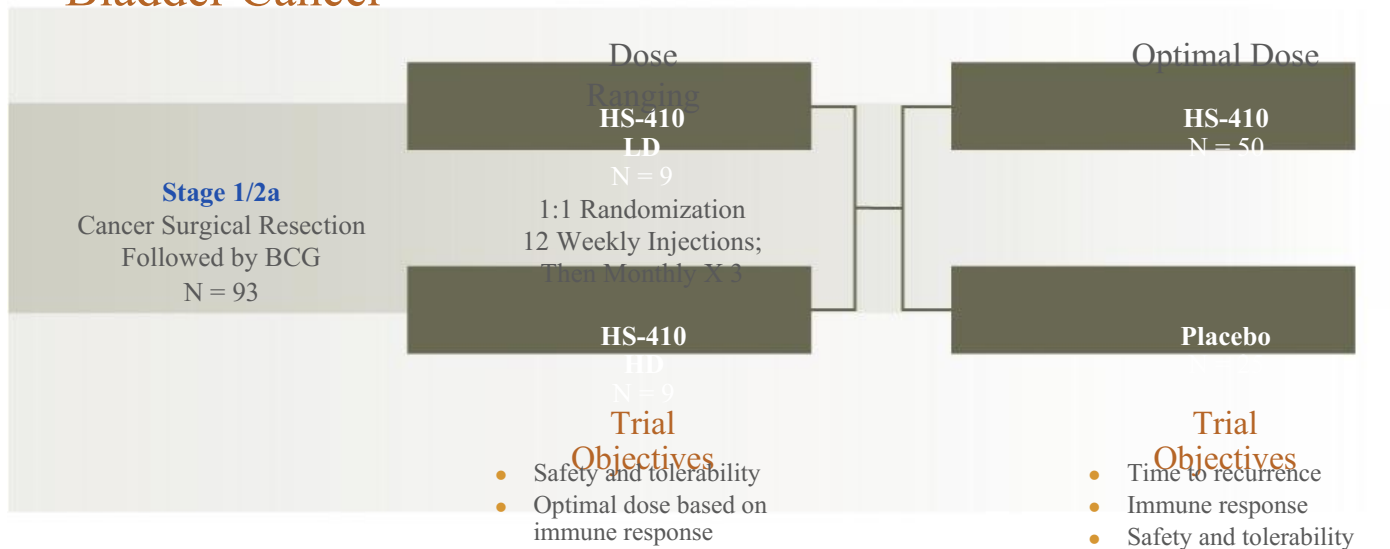
## In 2012 Alone, There Were 73,000 New Cases of Bladder Cancer Reported and 15,000 Deaths

- Currently-available treatments have high failure rate and are poorly tolerated
- Among highest lifetime treatment cost per patient of any cancer due to a high recurrence rate
- Opportunity to treat patients with minimal residual disease
- Drug manufacturing and preparation of IND and protocol for HS-410 in progress
- No new drugs for this patient population in >25 years
- HS-410 Phase 1/2 trial scheduled to begin in Q3 of 2013 and will include ~100 patients



# HS-410: Phase 1/2 Clinical Trial Design

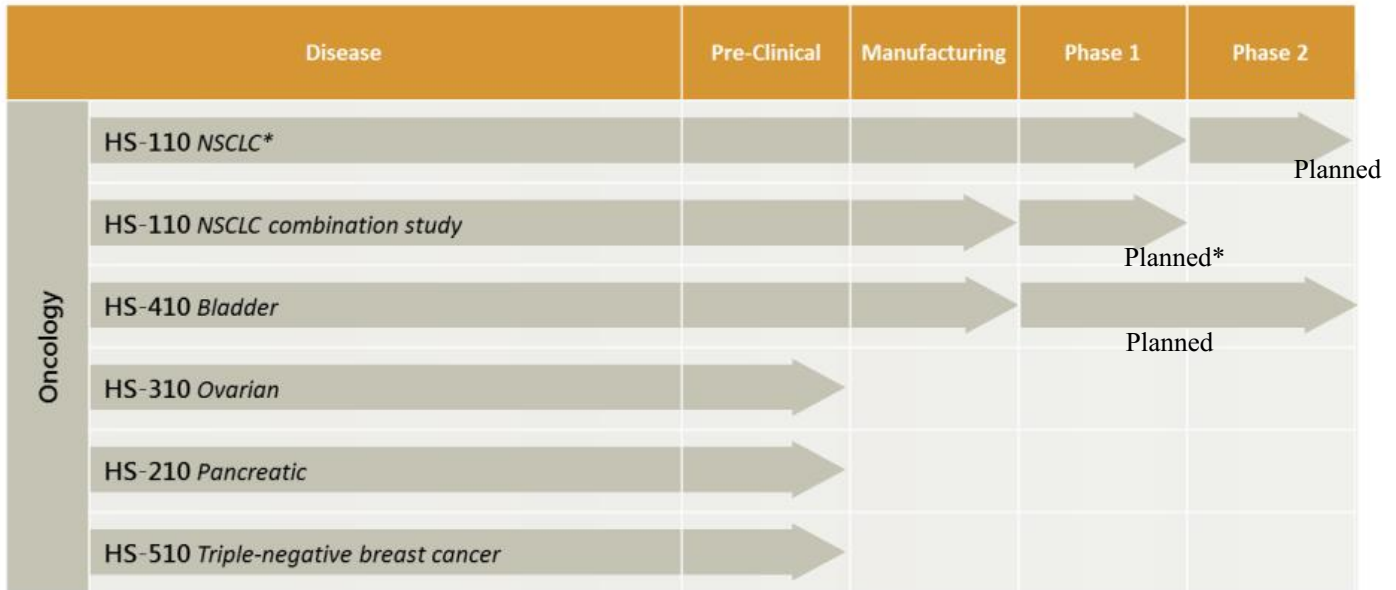
## Bladder Cancer



- HS-410 administered within existing standard of care guidelines
- Majority of cases are superficial (non-muscle invasive), treated with surgery followed by 6 weeks of interstitial BCG therapy



# Diverse Product Pipeline



\*Investigator-sponsored, grant-funded study



# IPO Milestones and Upcoming Events

	2013				2014			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
<b>HS-110</b> Lung Cancer			Phase 2 Clinical Trial ~120 Patients					
<b>HS-410</b> Bladder Cancer			Phase 1/2 Clinical Trial ~100 Patients					

**IPO funds will be used to progress two drug candidates to Phase 3 clinical trials**

## 2012 Milestones

- HS-110 lung cancer**
  - Phase 1 trial completion and publication\*
  - Phase 2 protocol design
  - HS-110 GMP manufacturing
- HS-410 Bladder Cancer**
  - Cell line development
  - Phase 1/2 protocol design

## 2013 Milestones

- HS-110 lung cancer**
  - Initiate 120 patient Phase 2 clinical trial
  - Phase 2 patient enrollment
- HS-410 Bladder Cancer**
  - Pre-IND FDA meeting
  - HS-410 scale manufacturing
  - Initiate 93 patient Phase 1/2 clinical trial
  - Complete stage 1 enrollment
  - Immune response data readout
- Corporate and other**
  - Enhance management team
  - Continued grant filings and notifications
  - Ovarian cancer cell line development

## 2014 Milestones

- HS-110 lung cancer**
  - Stage 1 enrollment completes
  - Immune response data readout
  - PFS data readout
- HS-410 Bladder Cancer**
  - Trial enrollment completes
  - Immune response data readout
  - Time-to-recurrence data readout
- HS-310 Ovarian Cancer**
  - File IND
  - First patient enrolled
  - Enrollment completes
  - Immune response data readout
- Corporate and other**
  - Continued grant filings and notifications
  - Various clinical publications

\*Investigator-sponsored, grant-funded study



# Immunotherapy Gaining Momentum

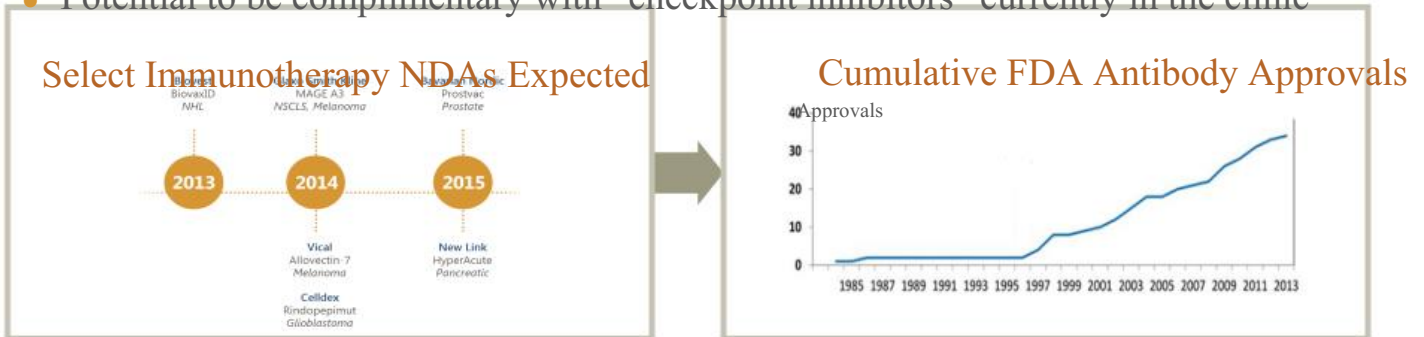
**Immunotherapy on the cusp of great industry breakthroughs with several BLA**

**approvals anticipated in coming years**

• Technology opening period for immunotherapies may be similar to antibodies

**Highly-novel approach to activate cytotoxic T-cells against multiple tumor antigens simultaneously**

• Potential to be complimentary with “checkpoint inhibitors” currently in the clinic



**“In a decade immunotherapy cancer drugs will be treating 60% of cancers and generating annual sales of up to \$35 billion.”— Andrew Baum, MD**

*Head of Global Healthcare Research, Celgene*

## Select Immunotherapy and Oncology-Focused Comparables

COMPANY	FOCUS	LEAD CATEGORY	STAGE OF DEVT	VALUATION
Heat Biologics	Live T-cell vaccine platform	NSCLC	Phase 2 (Post IPO)	~\$70M
Newlink Genetics	Live-cell vaccines	Pancreatic	Phase 3	\$556M
Stemline	Cancer stem cells	Leukemia	Phase 1/2	\$304M
Verastem	Cancer stem cells	Ovarian	Phase 1/2	\$270M
Infinity Pharma	Small molecules	NSCLC	Phase 2	\$901M
Array Biopharma	Small molecules	Multiple Myeloma	Phase 2	\$571M
Celldex	APC targeted immunotherapies	Glioblastoma	Phase 3	\$1.2B
Clovis Oncology	EGFR inhibitor	NSCLC	Phase 1	\$1.6B
Puma Biotech.	Tyrosine kinase inhibitor	Breast	Phase 2	\$1.2B
Immunocellular	Autologous dendritic cell vaccine	Glioblastoma	Phase 2	\$114M
Okairos	T-cell vaccine platform	----	Preclinical	\$323M GSK Buyout
Biovax	Modified virus injected into tumor	Melanoma	Phase 3	Up to \$1B (\$425M up to Heat Biologics Buyout) Heat Biologics * Valuation as 6-24-13

# Capitalization Structure

CAPITALIZATION STRUCTURE	SHARES	% OUTSTANDING
Common Stock*	3,583,654	84%
Stock Options	662,543	15%
Warrants	53,159	1%
Fully Diluted Shares Outstanding	4,299,356	100%

\*Assuming all preferred stock converts to common stock as of May 21, 2013



# Summary

## Clinical Stage Platform Technology Generating Promising Human Data

<p><b>Transformational Technology Platform</b></p>	<p><b>Unleashes the immune system against a wide range of cancers</b></p> <ul style="list-style-type: none"><li>• Over a decade of published research and recent clinical data</li></ul>
<p><b>Encouraging Clinical Data</b></p>	<p><b>Data to Date Demonstrate:</b></p> <ul style="list-style-type: none"><li>• Positive safety profile</li><li>• Powerful, disease-specific immune activation</li><li>• Immune activation corresponds with increased overall survival in initial 15 patients</li></ul>
<p><b>Value Creating Milestones</b></p>	<p><b>Strong Clinical Pipeline</b></p> <ul style="list-style-type: none"><li>• Phase 2 NSCLC clinical trial and Phase 1/2 bladder cancer trial following IPO with additional IND submissions planned</li><li>• Near-term enrollment and data readouts</li></ul>





**Heat Biologics**

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