Forward Looking Statements

This presentation includes statements that are, or may be deemed, “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. 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, the strength and breadth of our intellectual property, our ongoing and planned preclinical studies and clinical trials, the timing of and our ability to complete clinical trials and make regulatory filings and obtain and maintain regulatory approvals for our product candidates, our ability to partner our product development, 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 Annual Report on Form 10-K/A for the year ended December 31, 2018, our quarterly reports on Form 10-Q for the subsequent quarters and our other subsequent filings with the Securities and Exchange Commission (collectively, our “SEC Filings”). 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.
Snapshot of Heat Biologics (Nasdaq: HTBX)

- Biopharmaceutical company developing a suite of potential first-in-class immunotherapy products
- Promising pipeline based on T-cell activation and co-stimulation
- HS-110, an “off the shelf” cell-based immunotherapy product that has the potential to improve PD(L)-1 based therapy
  - Fully allogeneic product with low COGs
  - Ongoing Phase 2 program demonstrates signals of efficacy in two treatment settings
  - Broad market potential in multiple oncology indications
- Experienced management team with proven track record advancing oncology drugs to the market
<table>
<thead>
<tr>
<th>Product</th>
<th>MOA (Modality)</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>HS-110</td>
<td>gp96 (Cell Therapy)</td>
<td>NSCLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HS-130</td>
<td>OX40L (Cell Therapy)</td>
<td>Multiple Solid Tumor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTX-35</td>
<td>TNFRSF25 (mAb)</td>
<td>Multiple Solid Tumor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Introducing gp96 – Its dual role

The Immune System’s “Swiss Army Knife”*

“A Molecular Warning System”

- A natural biological process to deliver proteins (antigens) & gp96 to our immune system
- Gp96 “chaperones” newly-created proteins to the cell membrane where they are released and embedded
- Gp96 chaperoned proteins are only naturally released via necrosis
- Gp96, when present outside the cell, alerts the immune system and then becomes one of the most powerful adjuvants that show exclusive specificity to CD8+ (“killer”) T-cells

Heat’s T Cell Activation Platform - ImPACT®

“Severing the Leash”

Heat Biologics ImPACT® technology reprograms cancer cells to continuously secrete their own antigens

- **ImPACT® technology** genetically modifies tumor cells by “severing the leash” that binds the gp96 to the endoplasmic reticulum, and replacing it with a secretory sequence that pumps gp96 out of the cell

- **Mimics necrotic cell death** by enabling fully-allogeneic “off-the-shelf” living cancer cells to “pump-out” their own antigens along with their gp96 chaperone
Heat’s unique cell-secreted gp96 firstly activates dendritic cells via TLR signaling and subsequently CD8+ T cells via antigen cross presentation.

Activated cells EXPRESS chaperoned antigens. Chaperoned antigens activate dendritic cells, which then ACTIVATE & PROLIFERATE CD8+ T-cells. CD8+ T-cells locate and ELIMINATE cancer cells. T-cells circulate to destroy patient’s tumor.

Cluster of five 0.1 mL intradermal injections.
HS-110 Generates an Adaptive Immune Response

2 signals Delivered to APCs:
- Antigen cross presentation to MHC class I via CD91
- Up regulation of co-stimulatory signals via TLR2/4

1. **Secretion of gp96-Ig** carrying tumor specific proteins represented on the patients tumor
2. **Activation of APCs** (TLR2/4) and cross-presentation of antigens (CD91)
3. **Specific T-cell receptor** engagement
4. **Clonal Expansion** of Tumor Antigen Specific T cells.
HS-110 + Opdivo Combination Therapy

Potential to improve clinical responses and survival, without additional toxicity

Source: BMS images
HS-110 Overview

• HS-110 is a Phase 2 cell-based immunotherapy administered in combination with PD-(L)1 therapies to improve clinical outcomes for NSCLC patients
  - Allogeneic cells with engineered gp96 to present 70+ different cancer testis antigens
  - Selectively activate CD8+ “killer” T cells
  - gp96 can up-regulate T-cell co-stimulation and maturation of antigen presenting cells (APCs)

• PD-(L)1 is approved for multiple cancers and combination approaches may enhance survival benefits

The combination of HS-110 and PD-(L)1 therapy may benefit patients that have progressed on prior PD-(L)1 therapy

PD(L)-1 Therapy is Approved for Multiple Cancers

Estimated Number of New Cases in 2018 Worldwide

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>2,093,876</td>
<td>11.6%</td>
</tr>
<tr>
<td>Breast</td>
<td>2,088,849</td>
<td>11.6%</td>
</tr>
<tr>
<td>Colorectum</td>
<td>1,849,518</td>
<td>10.2%</td>
</tr>
<tr>
<td>Prostate</td>
<td>1,276,106</td>
<td>7.1%</td>
</tr>
<tr>
<td>Stomach</td>
<td>1,033,701</td>
<td>5.7%</td>
</tr>
<tr>
<td>Liver</td>
<td>841,080</td>
<td>4.7%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>572,034</td>
<td>3.2%</td>
</tr>
<tr>
<td>Other cancers</td>
<td>8,323,793</td>
<td>46%</td>
</tr>
</tbody>
</table>

Data Source: Globocan 2018. Graph production by Global Cancer Observatory.
**Combination of HS-110 and PD(L)-1 therapy**

- HS-110 is designed to overcome mechanisms of immune evasion, thereby having the potential to enable effective treatment with PD(L)-1
  - Target to be effective in patients that generally do not benefit from PD(L)-1 therapy

*Pie chart for illustrative purposes and not drawn to scale*
Clinical Support for HS-110 + Nivolumab MOA

“Turning COLD Tumors HOT”

Combination treatment drives “killer” CD8+ T-cells deep into tumors

CD8+ TIL Infiltration Associated with Clinical Response

Data from Phase 1b/2 trial in advanced NSCLC patients treated by HS-110 + Nivolumab at >2L
HS-110 Clinical Data
A Phase 1b/2 Study of HS-110 in Combination with Multiple Treatment Regimens in Patients with NSCLC

This is a non-randomized, open-label study that assesses HS-110 in combination with nivolumab or pembrolizumab in four different patient populations with advanced NSCLC

**HS-110 + Nivolumab**

- A. 2+ line Checkpoint Inhibitor (CPI) naïve patients
- B. 2+ line patients that progressed following CPI treatment

**HS-110 + Pembrolizumab ± Pemetrexed**

- C. 1st line patients achieving SD/PR prior to pembrolizumab maintenance therapy
- D. 1st line patients achieving SD/PR prior to pembrolizumab + pemetrexed maintenance therapy

**Primary Endpoints**
- Cohort A & B: **ORR**
- Cohort C & D: **PFS**

**Secondary Endpoints**
- OS, PFS, DCR, DOR

**Exploratory Endpoints**
- Baseline CD8+ TILs
  (Low defined as ≤ 10% stromal CD8+ TILs)
- PD-L1 expression
  (Negative defined as < 1% on tumor cells)
- Peripheral blood tumor mutation burden count
  (Low defined as < 10 mutations/ Mb)
- ELISPOT cytokine analysis
A comparison with published literature in NSCLC patients treated with *nivolumab as a single agent*

<table>
<thead>
<tr>
<th></th>
<th>HS-110 + Nivolumab △</th>
<th>Nivolumab *</th>
<th>Nivolumab ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR</strong></td>
<td>20%</td>
<td>19%</td>
<td>20%</td>
</tr>
<tr>
<td><strong>DCR</strong></td>
<td>46%</td>
<td>44%</td>
<td>49%</td>
</tr>
<tr>
<td><strong>Median PFS</strong></td>
<td>1.9</td>
<td>2.3</td>
<td>3.5</td>
</tr>
<tr>
<td>(months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Median OS</strong></td>
<td>16.9</td>
<td>12.2</td>
<td>9.2</td>
</tr>
<tr>
<td>(months)</td>
<td>50% of pts still alive with median follow-up time of 17 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

△ Heat Biologics Cohort A interim results as of July 2019 data cut, n=46
Cohort A: CPI naïve pts treated by HS-110 + Nivolumab at ≥2L

Progression free survival (PFS) is significantly better in patients who experienced dermal injection site reaction, thus supporting the HS-110 mechanism of action.

**ISR**

**ISR** = Yes refers to patients who experienced at least one injection site reaction at any time during treatment (N = 26)

<table>
<thead>
<tr>
<th>ISR</th>
<th>N</th>
<th>Median PFS, 95% CI (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>26</td>
<td>6.1 (1.8, 11.8)</td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>1.7 (1.3, 4.4)</td>
</tr>
</tbody>
</table>

HR: 0.51 (95%CI: 0.26 - 0.97)

*p* = 0.042

As of July 2019 data cut
Overall survival (OS) is significantly better in patients who experienced dermal injection site reaction, thus supporting the HS-110 mechanism of action.

<table>
<thead>
<tr>
<th>ISR</th>
<th>N</th>
<th>Median OS, 95% CI (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>26</td>
<td>42.1 (15.8, 42.1)</td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>5.9 (1.4, 11.6)</td>
</tr>
</tbody>
</table>

HR: 0.14 (95%CI: 0.05 - 0.36)

p < 0.0001

ISR = Yes refers to patients who experienced at least one injection site reaction at any time during treatment.

As of July 2019 data cut
Cohort A: Stage III or IV advanced NSCLC patients
- A comparison with published literature in NSCLC patients treated with *nivolumab as a single agent*

### Summary of PFS and OS

<table>
<thead>
<tr>
<th></th>
<th>HS-110 + Nivolumab $^\Delta$</th>
<th>Nivolumab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (n=46)</td>
<td>ISR+ (n=26)</td>
</tr>
<tr>
<td><strong>Median PFS</strong></td>
<td>1.9</td>
<td>6.1</td>
</tr>
<tr>
<td><strong>Median OS</strong></td>
<td><strong>16.9</strong></td>
<td>42.1</td>
</tr>
</tbody>
</table>

- **All (n=46)**: 93% Non-squamous NSCLC and 7% Squamous NSCLC
- **ISR+ (n=26)**: Inclusion of ISR = injection site reaction.

### Notes:
- $^\Delta$ Heat Biologics Cohort A interim results as of July 2019 data cut. Subgroup analysis by ISR was retrospective.
- 1 ISR = injection site reaction. 2 CD8+ TIL = CD8+ tumor infiltration lymphocytes at baseline (High > 10%, Low ≤ 10%). 3 PD-L1 (Positive ≥ 1%, Negative < 1%). NR = Not reached. As of last data cut-off in July, 2019. Median follow-up time = 14.4 months.
HS-110 Clinical Data
A Phase 1b/2 Study of HS-110 in Combination with Multiple Treatment Regimens in Patients with NSCLC

This is a non-randomized, open-label study that assesses HS-110 in combination with nivolumab or pembrolizumab in four different patient populations with advanced NSCLC

**HS-110 + Nivolumab**
- A. 2+ line Checkpoint Inhibitor (CPI) naïve patients
- B. 2+ line patients that progressed following CPI treatment

**HS-110 + Pembrolizumab ± Pemetrexed**
- C. 1st line patients achieving SD/PR prior to pembrolizumab maintenance therapy
- D. 1st line patients achieving SD/PR prior to pembrolizumab + pemetrexed maintenance therapy

**Primary Endpoints**
- Cohort A & B: ORR
- Cohort C & D: PFS

**Secondary Endpoints**
- OS, PFS, DCR, DOR

**Exploratory Endpoints**
- Baseline CD8+ TILs
  (Low defined as ≤ 10% stromal CD8+ TILs)
- PD-L1 expression
  (Negative defined as < 1% on tumor cells)
- Peripheral blood tumor mutation burden count
  (Low defined as < 10 mutations/ Mb)
- ELISPOT cytokine analysis
Cohort B: 
*CPI progressors treated by HS-110 + Nivolumab at ≥2L

Response and Disease Control
Comparison with Published Data

Tumor shrinkage observed in 38% of patients

*Waterfall plot of evaluable ITT patients (N=52) using RECIST 1.1 Target Lesion Response. Post-baseline scans not available for 4 patients.

<table>
<thead>
<tr>
<th></th>
<th>HS-110 + Nivolumab Δ</th>
<th>Nivolumab †</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR</strong></td>
<td>14% (8)</td>
<td>13% (7)</td>
</tr>
<tr>
<td><strong>PR</strong></td>
<td>14% (8)</td>
<td>13% (7)</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>46% (26)</td>
<td>46% (26)</td>
</tr>
<tr>
<td><strong>Not Evaluable</strong></td>
<td>7% (4)</td>
<td>7% (4)</td>
</tr>
<tr>
<td><strong>DCR</strong></td>
<td>61% (34)</td>
<td>59% (33)</td>
</tr>
</tbody>
</table>

Δ Heat Biologics Cohort B as of July 2019 data cut; n=56. PR unconfirmed as study is actively ongoing at time of analyses. Per iRECIST, one patient achieved confirmed PR after initial radiographic PD.


As of July 2019 data cut
As of July 2019 data cut

Cohort B: CPI progressors treated by HS-110 + Nivolumab at ≥2L

PFS by Injection Site Reaction (ISR)

ISR = Yes refers to patients who experienced at least one injection site reaction at any time during treatment (N = 39)

<table>
<thead>
<tr>
<th>ISR</th>
<th>Median PFS, 95% CI (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (n=39)</td>
<td>3.7 (1.9, 5.8)</td>
</tr>
<tr>
<td>No (n=17)</td>
<td>1.8 (1.0, 3.7)</td>
</tr>
</tbody>
</table>

HR: 0.40 (95% CI: 0.20 – 0.78)

p = 0.0068
Cohort B:

**CPI progressors treated by HS-110 + Nivolumab at ≥2L**

OS by Injection Site Reaction (ISR)

**ISR**

- Yes (n=39) 12.0 (9.4, Not Reached)
- No (n=17) 5.0 (3.0, Not Reached)

**HR:** 0.16 (95% CI: 0.05 – 0.45)

*p* = 0.0005

*ISR = Yes* refers to patients who experienced at least one injection site reaction at any time during treatment (N = 39)

As of July 2019 data cut
Summary of PFS and OS
Compared with Published Data

- Unresectable or metastatic NSCLC patients, heavily pretreated (63% with ≥ 2 lines of prior therapy)
- A comparison with published literature in NSCLC patients after PD-(L)1 progression

<table>
<thead>
<tr>
<th></th>
<th>HS-110 + Nivolumab</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>at ≥ 2nd line after CPI failure</td>
<td>at ≥ 3rd line after CPI failure</td>
</tr>
<tr>
<td>(Months)</td>
<td>All (n=56)</td>
<td>ISR+ (n=39)</td>
</tr>
<tr>
<td>Median PFS</td>
<td>3.2</td>
<td>3.7</td>
</tr>
<tr>
<td>Median OS</td>
<td>11.8</td>
<td>12.0</td>
</tr>
</tbody>
</table>

Δ Heat Biologics Cohort B as of July 2019 data cut estimate with 70% of the patients still alive. ORR and DCR unconfirmed as study is actively ongoing at time of analyses. ORR performed locally by study Investigators using RECIST 1.1.
† Single agent chemotherapy, Constatini et al 2018 ERJ Open Research ‡ Schvartsman et al 2017 Lung Cancer
Favorable Safety Profile to Date

• Over 1,000 doses administered to 150+ patients
• Only one patient ended treatment due to an HS-110 related non-serious adverse reaction *
• No treatment-related serious adverse reactions
• No increase in immune-related adverse events compared to single-agent checkpoint inhibitors

No additive toxicities to standard of care

*Represents the only patient of 150+ patients dosed who discontinued treatment for a HS-110 related adverse event

As of last data cut in 2019
## Product Pipeline

<table>
<thead>
<tr>
<th>Product</th>
<th>MOA (Modality)</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>HS-110</td>
<td>gp96 (Cell Therapy)</td>
<td>NSCLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HS-130</td>
<td>OX40L (Cell Therapy)</td>
<td>Multiple Solid Tumor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTX-35</td>
<td>TNFRSF25 (mAb)</td>
<td>Multiple Solid Tumor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
HS-130 Overview

• HS-130 is the first allogeneic, off-the-shelf, cell therapy approach utilizing OX40-mediated co-stimulation to enhance activation of dormant immune signal
  - Leverage HS-110 clinical experience and manufacturing know-how
  - Addition of OX40L fusion protein to extend and expand T cell memory
  - IND clearance by US FDA. Phase 1 expected to commence in Q4/2019

• Mechanism of Action offers broad market potential

• Heat Biologics has worldwide rights
# Product Pipeline

<table>
<thead>
<tr>
<th>Product</th>
<th>MOA (Modality)</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>HS-110</td>
<td>gp96 (Cell Therapy)</td>
<td>NSCLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HS-130</td>
<td>OX40L (Cell Therapy)</td>
<td>Multiple Solid Tumor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTX-35</td>
<td>TNFRSF25 (mAb)</td>
<td>Multiple Solid Tumor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
PTX-35 Overview

- Potential first-in-class T cell co-stimulator targeting TNFRSF25, with preferential specificity to generate “memory” CD8+ T cells
  - FDA clearance of PTX-35 IND expected in Q2, 2020
- Broad market potential
  - Efficacy demonstrated in multiple preclinical in vivo colon, lung and breast cancer models
- Synergistic combination with immunotherapies including HS-110 and CPIs
- Awarded a $15.2M grant to fund 70 pt. clinical trial
- Heat Biologics has worldwide rights
PTX-35 Preclinical Data highlights CD8+ T-cell Specificity
TNFRSF25 is preferentially expressed on CD8+ T-cells compared to other T-cell co-stimulators

• Co-stimulation occurs only in the context of **TCR recognition of antigen**
• Drives the development of **antigen-specific CD8+ T-cells**
  (mimics TL1A, the specific ligand of TNFRSF25)

In mice, TNFRSF25 agonists increases

- Antigen-specific T-cell proliferation
- Increased effector cytokine production
- Increased effector immune function
- Increased survival in mice model

**Compared to agonists OX40, GITR, 4-1BB:**
• TNFRSF25 shows superior activity in stimulating memory CD8+ cells in mice
• TNFRSF25 agonism plus **ImPACT** results in improved survival in mouse melanoma models
Heat Biologics

NASDAQ: HTBX

APPENDIX
HS-110

MOA AND PRECLINICAL DATA
PD(L)-1 Therapy is Approved for Multiple Cancers

Unlocking the Body’s Natural Defenses with a Broad Range of Combination Therapies

Heat’s Combination Platforms

**T-cell Activation**

*ImPACT® Therapy*
- Cell-based Delivery of Multiple Antigens
- Activation of Patients’ CD8+ “Killer” T-cells

*ComPACT™ Therapy*
- Cell-based Delivery of Multiple Antigens
- Activation of Patients’ CD8+ “Killer” T-cells

**Co-Stimulation**

*Pelican PTX-35 Monoclonal Antibody*
- Co-Stimulation to Enhance T-cell Activation and Expansion

**Checkpoint Inhibitors**
- PD1/PDL1
- CTLA-4
- Lag-3
- TIM-3
- Plus others

Combined with

Heat Technologies
HS-110 Mechanism of Action

2 signals delivered to APCs:

- Antigen cross presentation to MHC class I via **CD91**
- Up regulation of co-stimulatory signals via **TLR2/4**

1. **Secretion of gp96-Ig** carrying tumor specific proteins represented on the patients tumor
2. **Activation of APCs (TLR2/4)** and cross-presentation of antigens (CD91)
3. **Specific T-cell receptor** engagement
4. **Clonal Expansion** of Tumor Antigen Specific T cells.
HS-110 Mechanism of Action

- HS-110 is derived from a lung adenocarcinoma cell line transfected with gp96-Ig, where the gp96 KDEL ER retention sequence is replaced by IgG1 Fc.

- gp96-Ig acts as a chaperone protein for tumor associated antigens and is recognized by CD91 on APCs; resulting in cross-presentation of antigen to MHC I for the selection of antigen-specific CD8 cells.

- gp96-Ig also binds to TLRs 2 and 4 leading to upregulation of co-stimulatory molecules, which include MHC II and secretion of cytokines and chemokines.
ImPACT® “Off-the-shelf” Manufacturing

Designed for Robust, Pan-antigen T-cell Activation

- Frozen, fully-diluted single-dose vial
- Final drug product: 10 million cells
- Easily scaled manufacturing

Low COG, off-the-shelf alternative to autologous therapies
• Response rate by RECIST 1.1
  - Objective response rate (ORR) was 13%
  - Disease control rate (DCR) was 59%

• Median overall survival (OS) was estimated at 11.8 months with 70% of patients still alive

• Median progression free survival (mPFS) was 3.2 months

• Patients who experienced an ISR vs. those who did not:
  - Improved PFS (HR = 0.40, p = 0.0068)
  - Improved OS (HR = 0.16, p = 0.0005)

• The effect of HS-110 in combination with nivolumab is not dependent on PD-L1 expression

• Combination of HS-110 and nivolumab was well tolerated by patients
PTX-35

PRECLINICAL DATA
### TNFRSF25
An Emerging Target for T-cell Co-stimulation

<table>
<thead>
<tr>
<th>Target</th>
<th>Companies</th>
<th>Co-stimulator Combinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-1BB</td>
<td>Pfizer, ISA Pharma, Gilead, Bristol Myers, Inhibrx, Immatics, Pieris, NCI MedImmune, GSK, Incyte, Phase 1/2</td>
<td>Phase 1/2 Combinations: Chemotherapy, epigenetic modulator, CD20 mAb, HPV vaccine, CART, PD-L1, BTK, Herceptin, modified CD8+ T cells, IL-2, CSF1R, LAG-3, bispecific w/ HER-2, two co-stimulators (w/ OX40)</td>
</tr>
<tr>
<td>OX40</td>
<td>Genentech, Pfizer, AbbVie, Bristol Myers, Alligator Bio Novartis, Incyte-Agenus, MedImmune, GSK, Incyte, Phase 1</td>
<td>OX-40 prior to surgery. Other combinations: PD-1, PD-L1, CTLA4, axitinib, 41BB, smoothened inhibitor Anti-CD33, azacitidine, TLRs, bi-specifics of OX40 and CTLA-4</td>
</tr>
<tr>
<td>GITR</td>
<td>MedImmune, GSK, Incyte, Phase 1</td>
<td>Phase 1 Combinations: PD-1, Fc disabled co-stimulation, hexameric GITR ligand, IDO inhibitor, CTLA-4, GITR ligand-fusion</td>
</tr>
<tr>
<td>CD27</td>
<td>Celldex-BMS, Merck, Aduro</td>
<td>Phase 1/2 Combinations: PD-1/L-1, sunitinib, CD20, melanoma vaccine, TL3 agonist</td>
</tr>
<tr>
<td>ICOS</td>
<td>Celgene-Jounce, GSK</td>
<td>Phase 1/2 Combinations: PD-1, CTLA4, docetaxel</td>
</tr>
<tr>
<td>TNFRSF25 Heat (under Pelican)</td>
<td>FDA clearance of PTX-35 IND expected in Q2, 2020 in advanced solid tumors</td>
<td></td>
</tr>
</tbody>
</table>

- TNFRSF25 is a potential best-in-class T cell co-stimulator due to its **preferential specificity to ‘memory’ CD8+ T cells**
- **Pelican is the only company** with a disclosed program targeting TNFRSF25
TNFRSF25 as a Novel I/O Combination Target

• TNFRSF25 is one of the most recently discovered T cell costimulator, and is a rapidly emerging target

• Pelican is the only company developing TNFRSF25 agonist antibodies for I/O

“Although TNFRSF25 is chromosomally localized with 4-1BB, OX40, GITR and CD27, sequence analysis suggests that TNFRSF25 is relatively divergent or perhaps ancestral... Thus we might expect that therapeutics directed against this pathway will have unique activity.”

_Citation: Mahoney K. et al. Nat Rev Drug Discov._ 2015
TNFRSF25’s evolutionary origin

*Potentially a mechanism that preserves needed tissue and friendly bacteria during an immune response*

Example: gut invasion occurs in the context of friendly microbiome bacteria. How does the body protect what is needed while weeding out invaders?

---

One molecule – three types of T-cells

Expand but delay activation of existing Treg

Expand activated CD8+

Inhibits Tconv to iTreg conversion

CD8

CD8

Treg

Treg

T Cell

APC

TL1a

TNFRSF25

CD4

iTreg

Heat Biologics
TNFRSF25 is preferentially expressed on CD8+ and CD4+ T-cells compared to other T-cell co-stimulators.

Genomics Institute of the Novartis Research Foundation Su et al. PNAS 2004:101(16);6062-7

*red* = high expression
Preferential CD8+ T-cell Induction with TNFRSF25 in Mice

Pre-clinical studies with murine agonist antibody shows TNFRSF25 preferentially ‘boosts’ CD8+ T-cells, whereas OX40 is preferential to CD4+ T-cells

The frequency of antigen-specific memory CD4+ or memory CD8+ T-cells following treatment of mice with ImPACT™ alone, or in combination with OX40 or TNFRSF25 antibodies

schreiber et al. J Immunol 2012:189(7);3311-8
TNFRSF25 agonist + *ImPACT* Significantly Increases Survival in Mice

Established (nine-day) B16-F10 melanoma mouse model

*Schreiber T. et al. SITC 2014*