**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**WASHINGTON, D.C. 20549**

**FORM 8-K**

**CURRENT REPORT**

**Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

Date of Report (date of earliest event reported): **June 24, 2019**

# Heat Biologics, Inc.

*(Exact name of registrant as specified in charter)*

**Delaware**
*(State or other jurisdiction of incorporation)*

| **001-35994** | **26-2844103** |
|---|---|
| *(Commission File Number)* | *(IRS Employer Identification No.)* |

**801 Capitola Drive**
**Durham, NC 27713**
*(Address of principal executive offices and zip code)*

**(919) 240-7133**
*(Registrant's telephone number including area code)*

**N/A**
*(Former Name and Former Address)*

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common Stock, $0.0002 par value per share | HTBX | The Nasdaq Capital Market |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by checkmark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 8.01 Other Events.**

Heat Biologics, Inc. (the "Company") will be making corporate presentations over the next several weeks. In connection with the presentations, the Company intends to discuss the new corporate slide presentation attached as Exhibit 99.1 hereto, which is incorporated herein by reference.

The slide presentation attached as Exhibit 99.1 to this Current Report on Form 8-K includes"safe harbor" language pursuant to the Private Securities Litigation Reform Act of 1995, as amended, indicating that certain statements contained in the slide presentation are "forward-looking" rather than historical.

The Company undertakes no duty or obligation to update or revise information included in this Current Report or the Exhibit.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits.

The following exhibit is filed with this Current Report on Form 8-K:

| Exhibit Number | Description |
|---|---|
| 99.1 | Corporate Presentation dated June 24, 2019 |

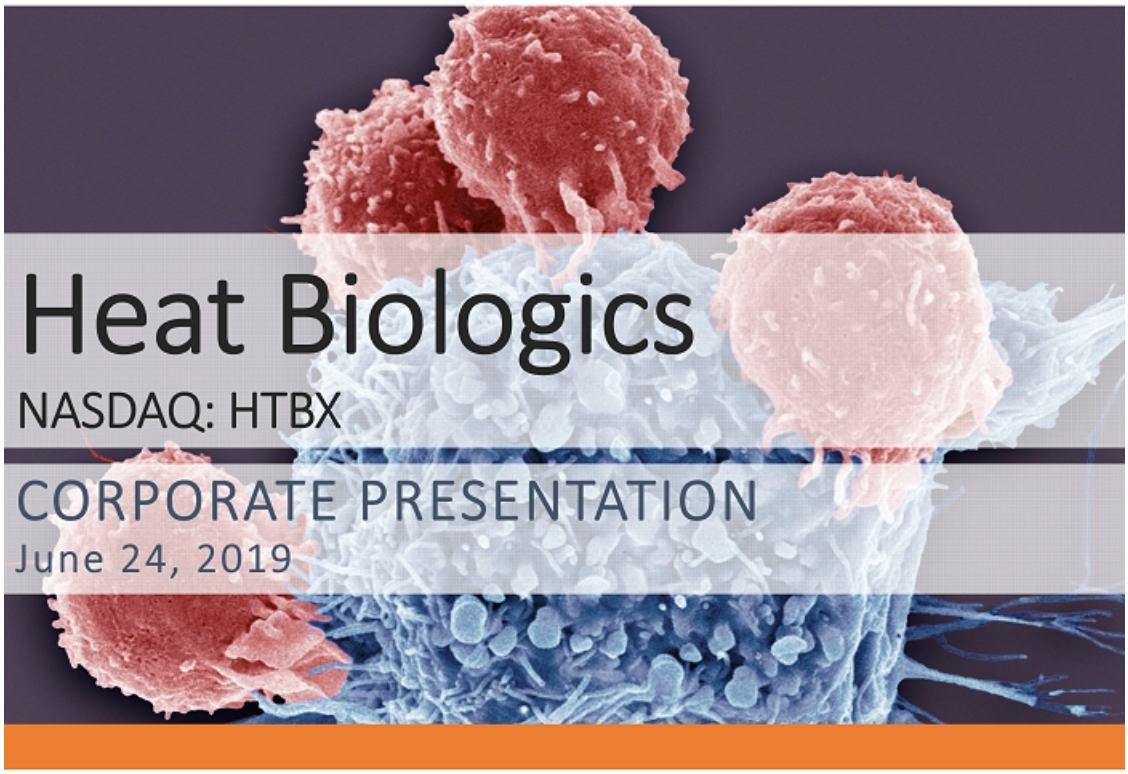
**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: June 24, 2019

HEAT BIOLOGICS, INC.

By: /s/ Jeffrey Wolf
Name: Jeffrey Wolf
Title: Chairman, President and Chief Executive Officer


Heat Biologics
Heat Biologics
NASDAQ: HTBX
CORPORATE PRESENTATION
June 24, 2019

# 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.

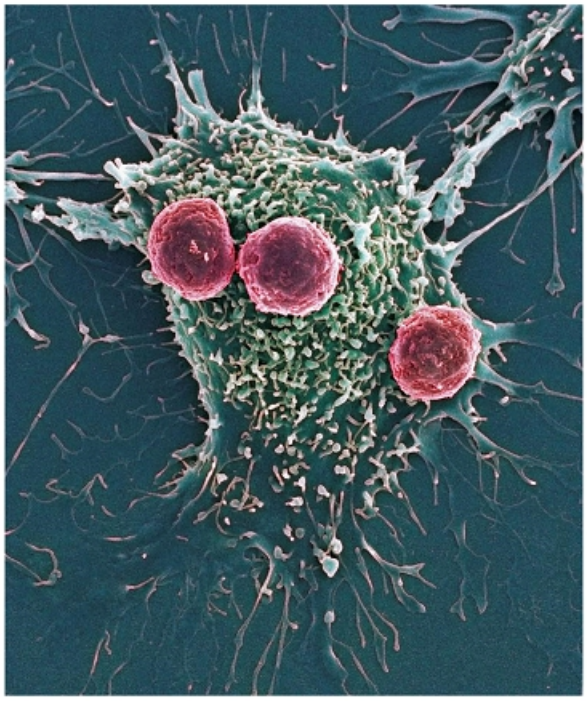
By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines 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.

Heat Biologics

# Our Mission

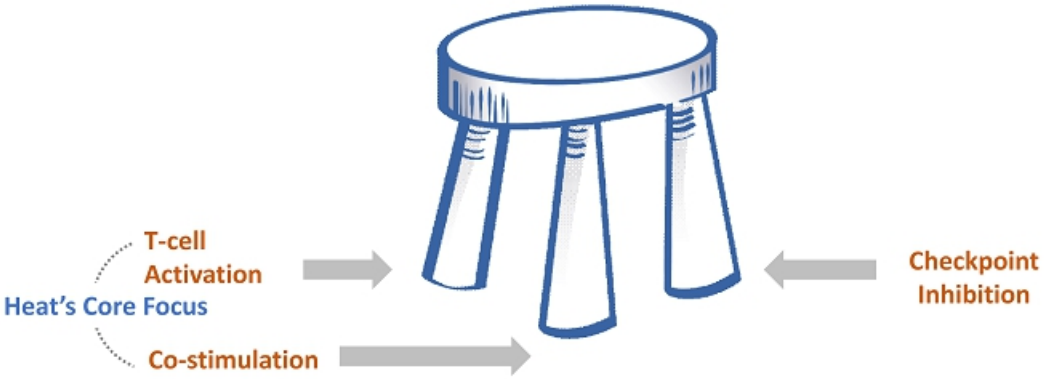
*To improve patient outcomes by developing more effective immunotherapies designed to*

*Turn "COLD" tumors "HOT*



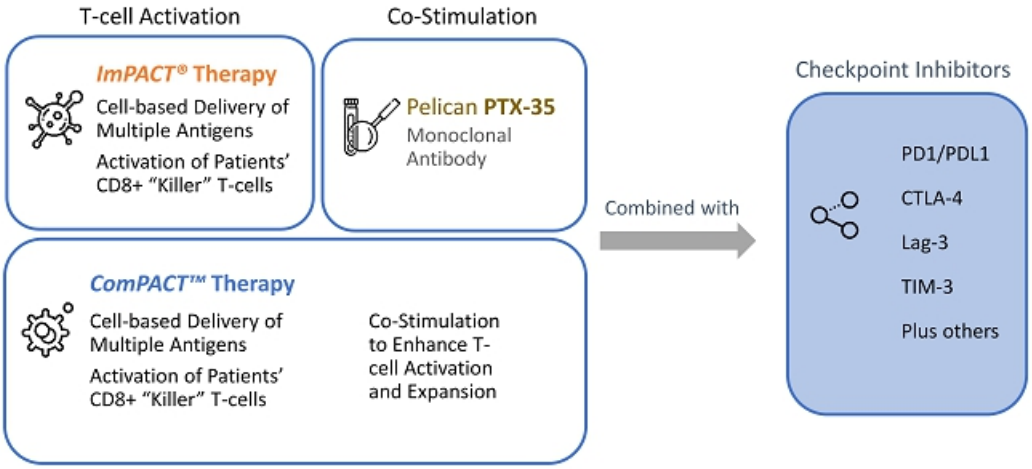
# Effective Immuno-Oncology Therapy

*The three legs of an Immuno-Oncology Stool*



# Heat's Combination Platforms

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




Heat Technologies

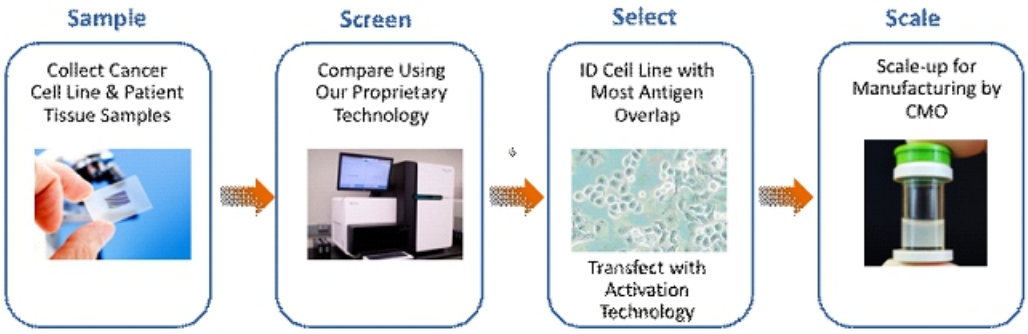
# Product Pipeline

*Combination Therapies Designed to Activate CD8+ T-cells Against Cancer*

| Combination Therapies | Indication | Pre-clinical | Phase 1 | Phase 2 | Phase 3 | Comments |
|---|---|---|---|---|---|---|
| *ImPACT®* HS-110 | NSCLC | | | → | | *ImPACT™* activation technology in combination with nivolumab and pembrolizumab |
| *ComPACT®* HS-130 | Multiple Solid Tumors | | → | | | *ComPACT™* activation technology in combination with checkpoint inhibitors |
| **Co-stimulators** | | | | | | |
| PTX-35 | Multiple Solid Tumors | | → | | | Humanized monoclonal antibody, functional agonist of human TNFRSF25 ($15.2M CPRIT grant) |

# *ImPACT® "Off-the-shelf"* Manufacturing

*Designed for Robust, Pan-antigen T-cell Activation*

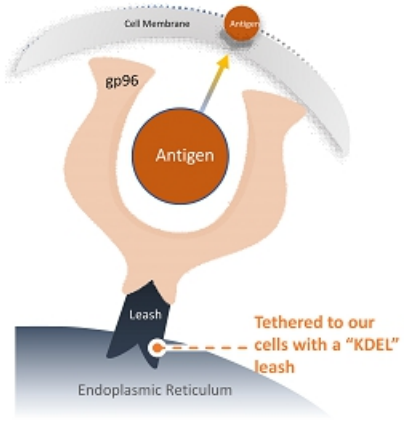



- Frozen, fully-diluted single-dose vial
- Final drug product: 10 million cells
- Easily scaled manufacturing

**Low COG, off-the-shelf alternative to autologous therapies**

# Introducing gp96 – Its dual role

*The Immune System's "Swiss Army Knife"**




**"Molecular Warning System"**

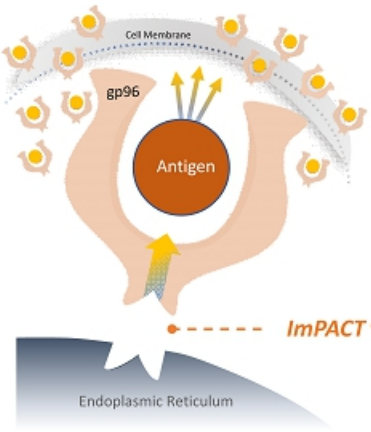
- A natural biological process to deliver proteins (antigens) & gp96 to our immune system
- Gp96 "chaperones" newly-created proteins to the cell membrane where they are released and embedded
- Gp96 chaperoned proteins are only naturally released via necrosis
- Gp96, when present outside the cell, alerts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

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

# Heat's T Cell Activation Platform - *ImPACT®*

*"Severing the Leash"*

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



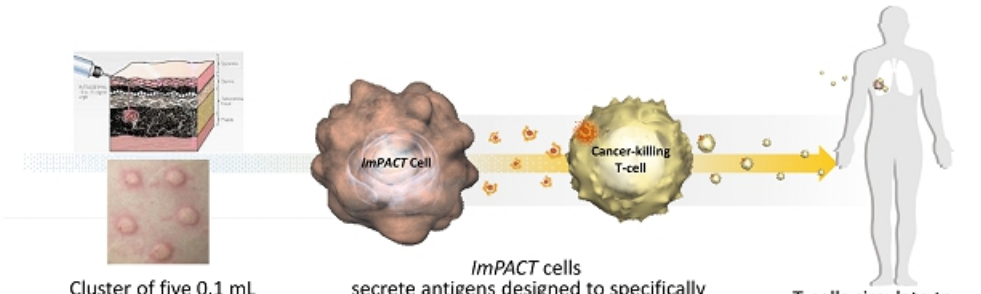

***ImPACT®* technology** genetically modifies tumor cells by "severing the leash" that binds the gp96 to the endoplasmic reticulum, and replacing it with a secretory sequence that pumps gp96 out of the cell

***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

***ImPACT* technology removes the leash that binds gp96 to the cell**

**Designed to activate a powerful pan-antigen cytotoxic T-cell immune response**

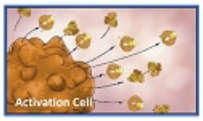
# *ImPACT®*: Immune Pan-antigen Cytotoxic Therapy



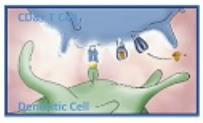

Cluster of five 0.1 mL intradermal injections

*ImPACT* cells secrete antigens designed to specifically activate patient's killer T-cells

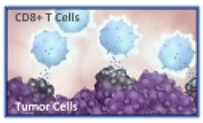
T-cells circulate to destroy patient's tumor




Activated cells **EXPRESS** chaperoned antigens


Chaperoned antigens activate dendritic cells, which then **ACTIVATE** & **PROLIFERATE** CD8+ T-cells



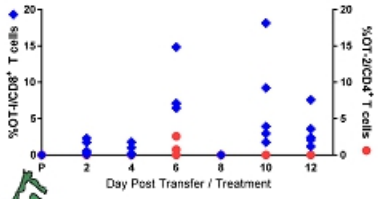

CD8+ T-cells locate and **ELIMINATE** cancer cells

Heat's unique cell-secreted gp96 firstly activates dendritic cells via TLR signaling and subsequently CD8+ T cells via antigen cross presentation

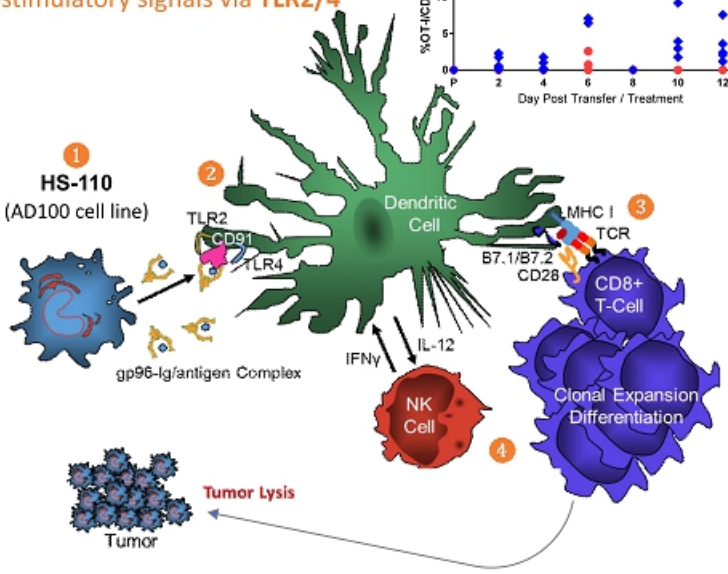
# HS-110 Generates an Adaptive Immune Response

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.



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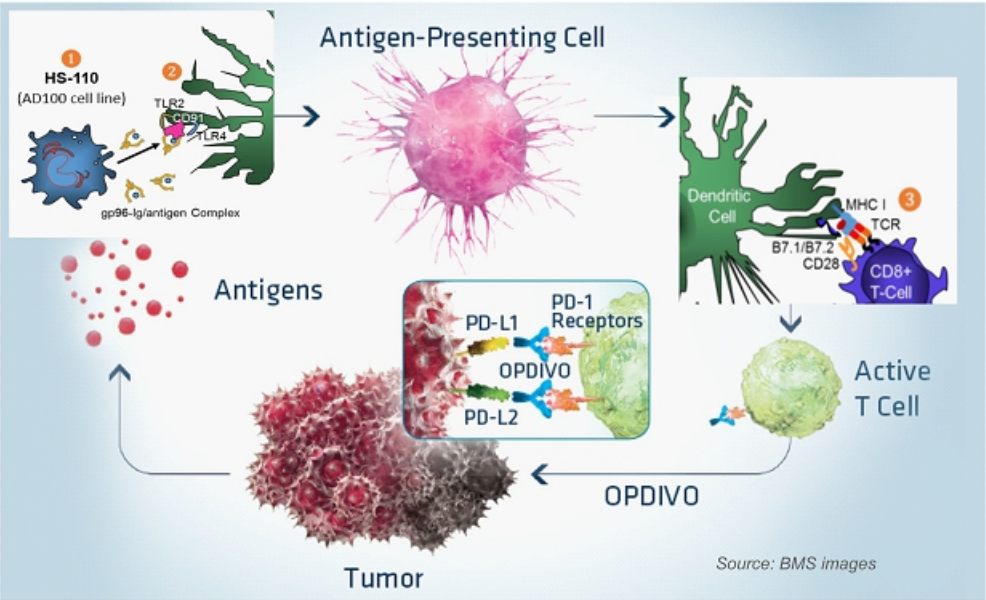
# HS-110 + Opdivo Combination Therapy

*Potential to improve clinical responses and survival, without additional toxicity*



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# HS-110 Trial Design

*A Phase 1b/2 study of HS-110 in combination with multiple treatment regimens for patients with non-small cell lung cancer (The "DURGA" Trial)*

| | Patient Treatment Setting | Treatment Arm | Cohort |
|---|---|---|---|
| Enroll | 2nd Line or Greater N = 100 | HS110 + Nivolumab | **Cohort A:** CPI naïve (N=40, including Phase 1b) |
| | | | **Cohort B:** CPI progressor (N=60) |
| | 1st Line Maintenance N = up to 20 | HS110 + Pembrolizumab +/- Pemetrexed | **Cohort C:** Maintenance pembrolizumab |
| | | | **Cohort D:** Maintenance pembrolizumab + pemetrexed |

**Primary Endpoints**

***Phase 1b:***
Safety

***Phase 2:***
Cohort A&B: ORR
Cohort C&D: PFS

**Secondary Endpoints**

OS, PFS, DCR, DOR

**Exploratory Endpoints**

Correlation of clinical outcomes to the following factors

- **Baseline CD8+ TILs**
  (Low defined as ≤ 10% stromal CD8+ TILs)
- **Baseline PD-L1 expression**
  (Negative defined as < 1% on tumor cells)
- **Peripheral blood tumor mutation burden**
  (Low defined as < 10 mutations / Mb)
- **ELISPOT cytokine analysis**

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# Cohort A: Patient Characteristics

Stage III or IV Advanced NSCLC Patients

| | | Cohort A (N = 42) |
|---|---|---|
| Median age (range) | | 64 (37-87) |
| Female gender | | 22 (52%) |
| Caucasian | | 38 (90%) |
| ECOG PS 1 | | 26 (62%) |
| Histology | Adeno | 39 (93%) |
| | Squamous | 3 (7%) |
| Smoking Status | Current/past | 37 (88%) |
| | Never | 5 (12%) |

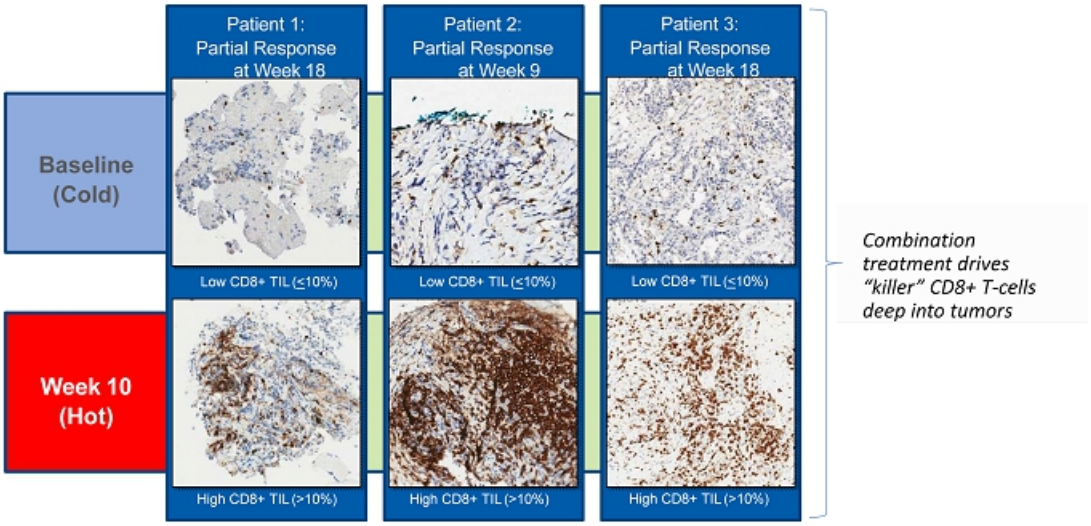
| | | Cohort A (N = 42) |
|---|---|---|
| EGFR or ALK positive | | 9 (22%) |
| Prior lines of Tx | 1 | 27 (64%) |
| | 2 or more | 13 (30%) |
| | Unavailable | 2 (5%) |
| PD-L1 | < 1% | 16 (38%) |
| | ≥ 1% | 13 (31%) |
| | Unevaluable | 13 (31%) |
| CD8+ TIL | ≤ 10% | 12 (29%) |
| | > 10% | 8 (19%) |
| | Unevaluable | 22 (52%) |

*As of last data cut-off in January, 2019*

Heat Biologics

# Clinical Support for HS-110 + Nivolumab Mechanism of Action

## *"Turning COLD Tumors HOT"*




CD8+ TIL Infiltration Associated with Clinical Response

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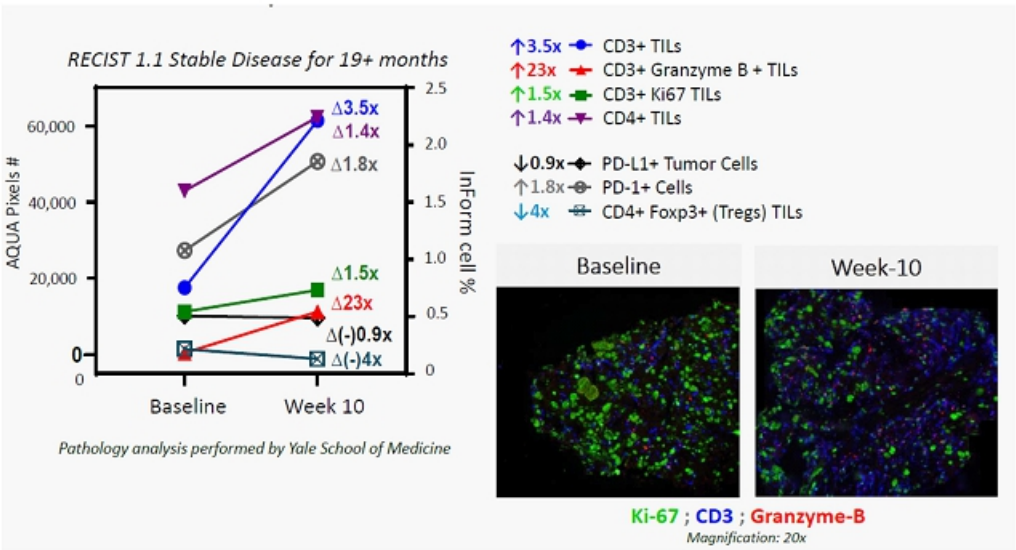
# Combination Treatment Substantially Increased Killing Activity in Patient Tumor Microenvironment




**Substantial increase of CD3+ TILs and CD3+ Granzyme B+ TILs for enhanced tumor killing activity**

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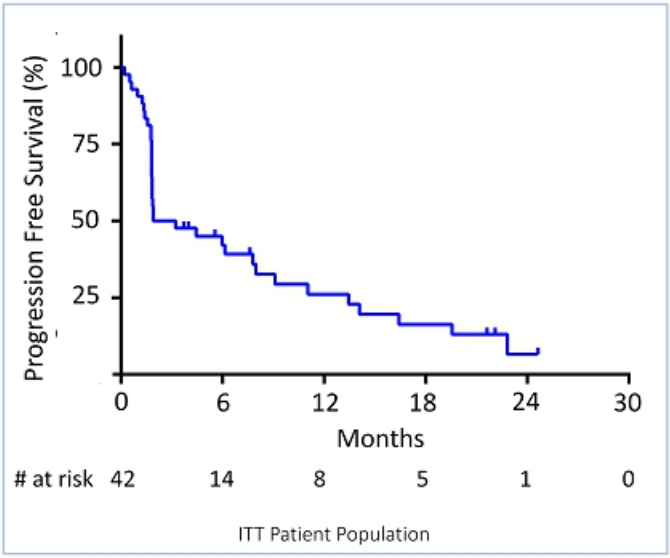
# Cohort A:

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

# Progression-Free Survival (PFS)




*As of last data cut-off in January, 2019*

**Median PFS**
**2.6 months**
(95% CI: 1.8 - 8 months)

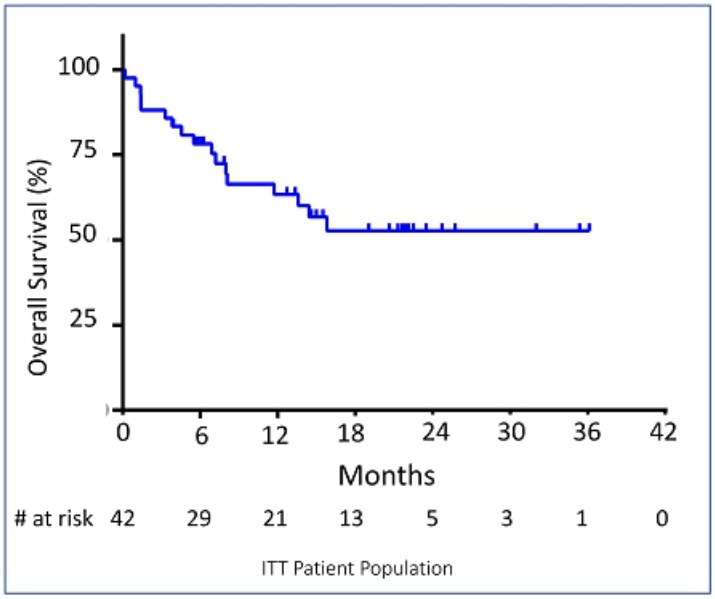
Median PFS of nivolumab alone
2.3 months *
(95% CI: 2.2 – 3.3 months)

* Borghaei et al. 2015 Nivolumab versus Docetaxel in Advanced Nonsquamous Non–Small-Cell Lung Cancer. *New England Journal of Medicine*

# Cohort A:

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

# Overall Survival (OS)




**Median OS**
**Not Reached**
(95% CI: 8.1 months - NR)

60% of patients still alive with median follow-up time of 14.4 months

Median OS of nivolumab alone 12.2 months*
(95% CI: 9.7 – 15.0 months)

*Borghaei et al. 2015 *NEJM*

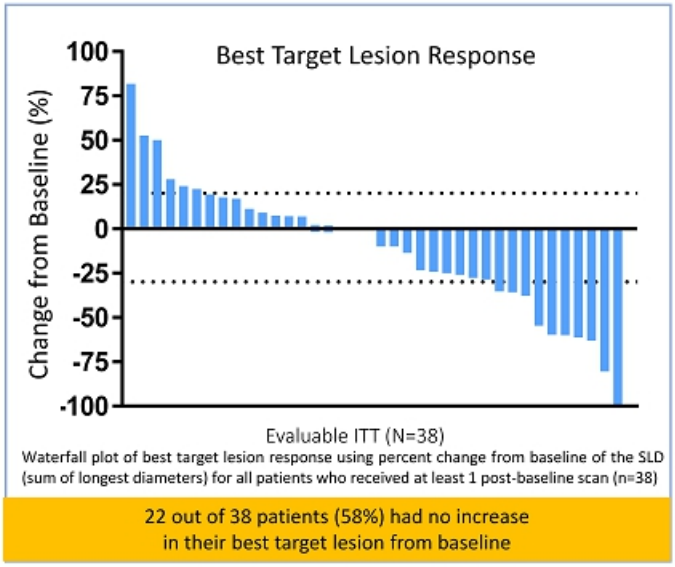
*As of last data cut-off in January, 2019*

Heat Biologics

# Cohort A:

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

# Best Overall Response




Waterfall plot of best target lesion response using percent change from baseline of the SLD (sum of longest diameters) for all patients who received at least 1 post-baseline scan (n=38)

22 out of 38 patients (58%) had no increase in their best target lesion from baseline

**RECIST 1.1 Objective Response Rate = 21.4%**
(95% CI: 10.3 - 36.8%)

| ITT (N=42) | |
|---|---|
| PR | 9 (21%) |
| SD | 12 (29%) |
| Not evaluable | 4 (10%) |
| **DCR** | **21 (50%)** |

Nivolumab alone in CPI naïve patients*
ORR = 19% (95% CI: 15% - 24%)
DCR = 44%

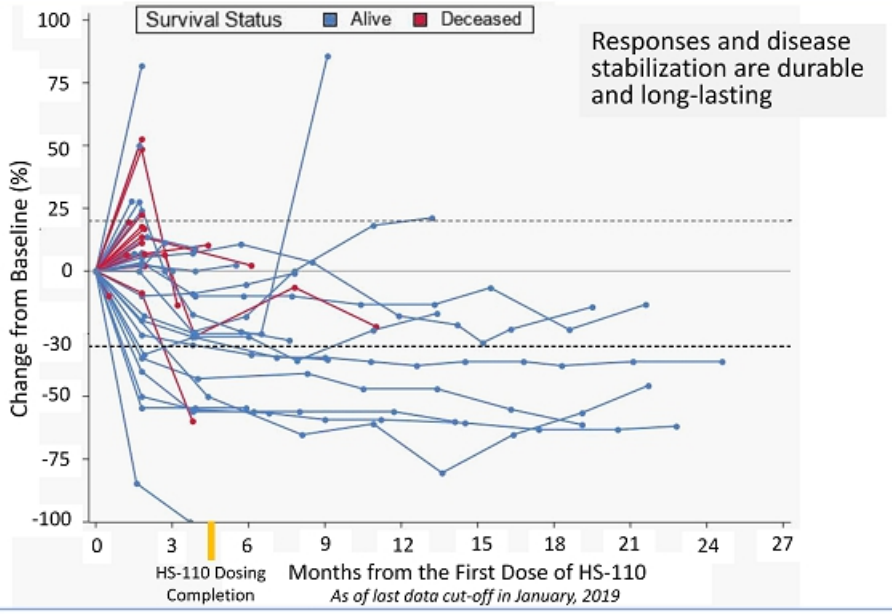
**Borghaei et al 2015 NEJM*

*As of last data cut-off in January, 2019*

# Cohort A:

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

## Duration of Benefit



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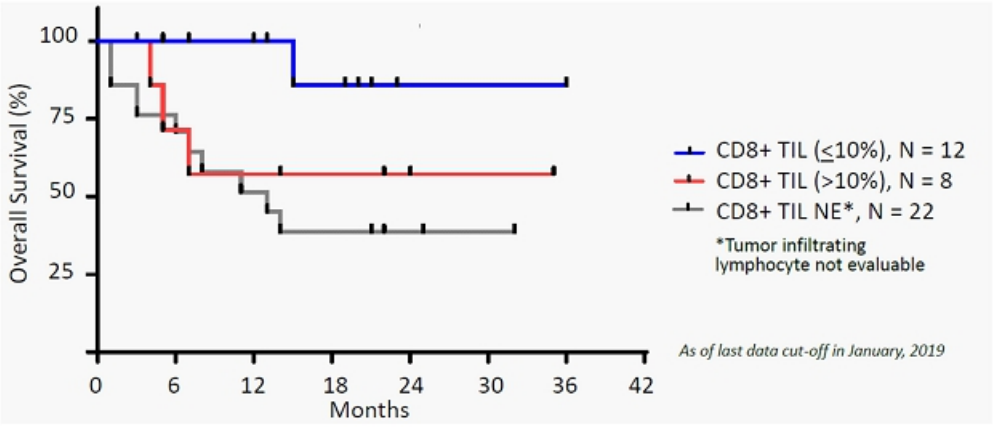
# Cohort A:

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

## Improved Survival in "Cold" Tumor Patients

*Overall Survival (OS) by Baseline CD8+ TIL*




- **Survival benefit observed in patients with low CD8+ TIL at baseline**, as compared to high CD8+ TIL at baseline, **HR = 0.39 (95% CI: 0.06 – 2.31)**
- Median overall survival not reached for both groups
- The above benefit is **contrary to what is expected** based on current literature

Gibney et al. Lancet Oncol. 2016 December ; 17(12): e542–e551

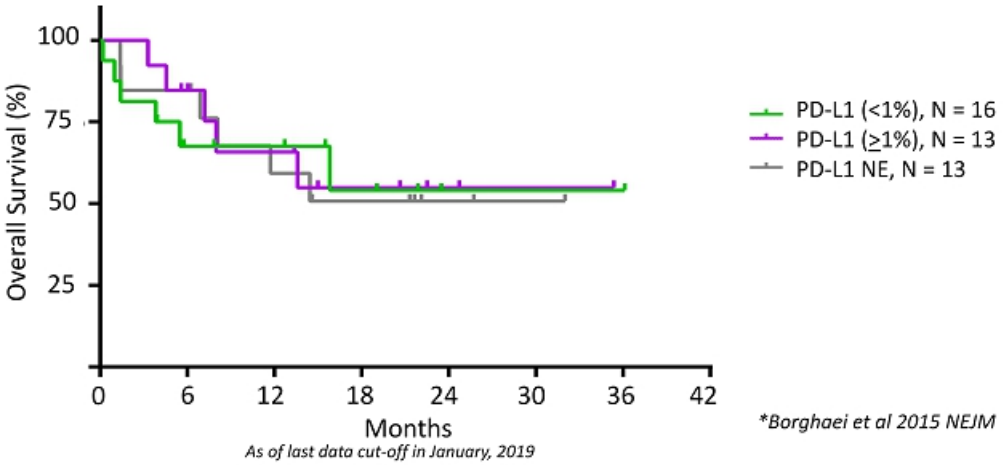
Heat Biologics

# Cohort A:

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

## Benefit Independent of PD-L1 Status

*Overall Survival (OS) by Baseline PD-L1 Status*




*As of last data cut-off in January, 2019*

**Borghaei et al 2015 NEJM*

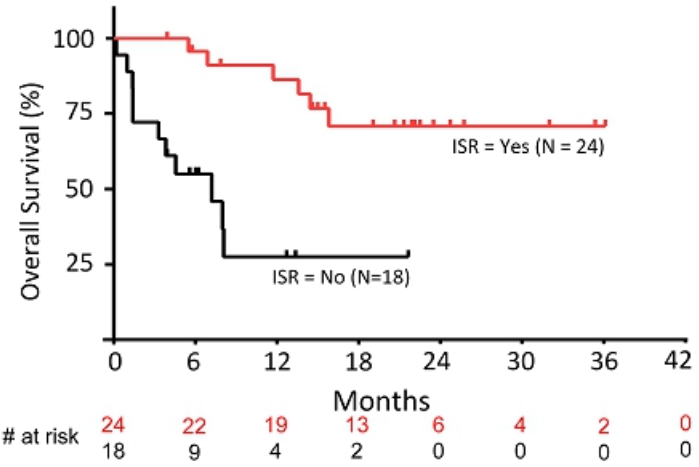
- **Our therapy is agnostic to PD-L1 status**
- Similar survival observed in both PD-L1 positive and PD-L1 negative patients **HR 0.85 (95% CI: 0.26 – 2.79)**
- For nivolumab alone, PD-L1 positive patients typically have better outcomes*

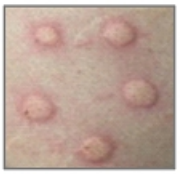
Heat Biologics

# Cohort A:

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

## OS by Injection Site Reaction (ISR)



Typical Injection Site Reaction

**mOS: NR vs. 7.2 months**
**HR: 0.15**
(95% CI: 0.05-0.45)
***p = 0.0001***

*As of last data cut-off in January, 2019*

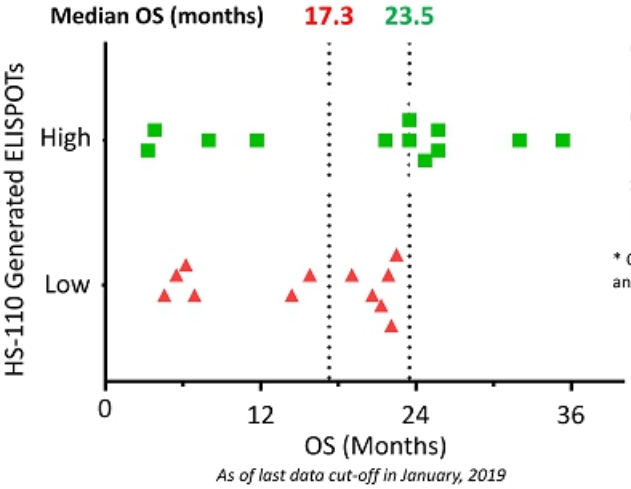
Survival is significantly better in patients who experienced dermal injection site reaction, thus supporting the HS-110 mechanism of action

Heat Biologics

# Cohort A:

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

## Survival Benefit with Increased Immune Activity




*As of last data cut-off in January, 2019*

**Over the course of treatment, patients* with higher levels of HS-110 elicited immune response from peripheral blood demonstrated a survival benefit of approximately 6 months**

* Only patients with blood samples available at baseline and during treatment were included in this analysis

**High** = Patients with absolute ELISPOT increases **above** the group median
**Low** = Patients with absolute ELISPOT increases **below** the group median

# Cohort B: Patient Characteristics

- Stage III or IV advanced NSCLC patients
- Patients were heavily pretreated (80% with 2+ lines of prior therapy)

| | | Cohort B (N = 20) |
|---|---|---|
| Median age (range) | | 65 (56-84) |
| Female gender | | 14 (70%) |
| Caucasian | | 15 (75%) |
| ECOG PS 1 | | 10 (50%) |
| EGFR or ALK positive | | 2 (10%) |
| Histology | Adeno | 17 (85%) |
| | Squamous | 3 (15%) |
| Smoking Status | Current/past | 17 (85%) |
| | Never | 3 (15%) |
| Prior lines of Tx | 1 | 3 (15%) |
| | 2 | 9 (45%) |
| | ≥ 3 | 8 (40%) |

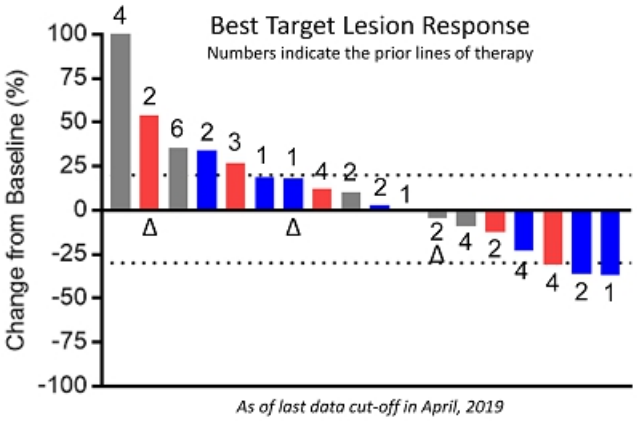
| | | Cohort B (N = 20) |
|---|---|---|
| PD-L1 | < 1% | 7 (35%) |
| | ≥ 1% | 8 (40%) |
| | Unevaluable | 5 (25%) |
| CD8+ TIL | ≤ 10% | 7 (35%) |
| | > 10% | 6 (30%) |
| | Unevaluable | 7 (35%) |
| Time (months) on prior CPI: Median (range) | | 10.2 (6, 19) |
| Time (months) between last CPI dose and study entry: Median(range) | | 1.7 (1, 21) |

*As of last data cut-off in January, 2019*

# Cohort B:

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

# Objective Response Rate




*As of last data cut-off in April, 2019*

**RECIST 1.1 ORR = 15%**
(95% CI: 3.2% - 37.9%)

Per investigator assessment:
**PR = 4 (20%)**
**SD = 7 (35%)**
**DCR = 11 (55%)**

CD8+ TIL High (> 10%)
CD8+ TIL Low (≤10%)
CD8+ TIL Unevaluable

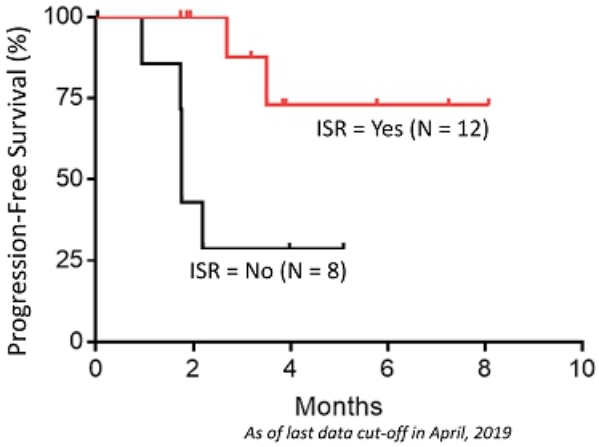
The majority of patients had adenocarcinoma
Δ indicates patients with squamous cell carcinoma

- Stabilization of disease in > 50% of patients
- Tumor shrinkage observed in 35% of patients
- Signal of efficacy observed in patients that have failed multiple therapies
- Benefit observed in patients with "cold" tumor at baseline (CD8+ TIL ≤ 10%)

# Cohort B:

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

## PFS by Injection Site Reaction (ISR)




*As of last data cut-off in April, 2019*

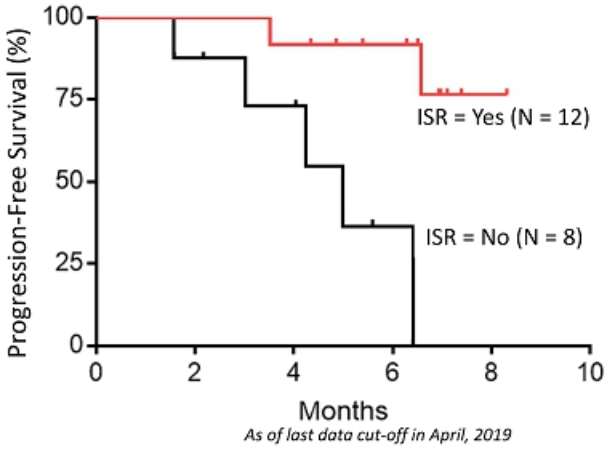
**mPFS: NR vs. 1.8 months**
**HR = 0.17** (95% CI, 0.03-0.84)
***p = 0.013***

PFS is significantly better in patients who experienced dermal injection site reaction, thus supporting the HS-110 mechanism of action

# Cohort B:

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

## OS by Injection Site Reaction (ISR)




*As of last data cut-off in April, 2019*

**mOS: NR vs. 5 months**
**HR = 0.13** (95% CI, 0.02-0.71)
***p = 0.002***

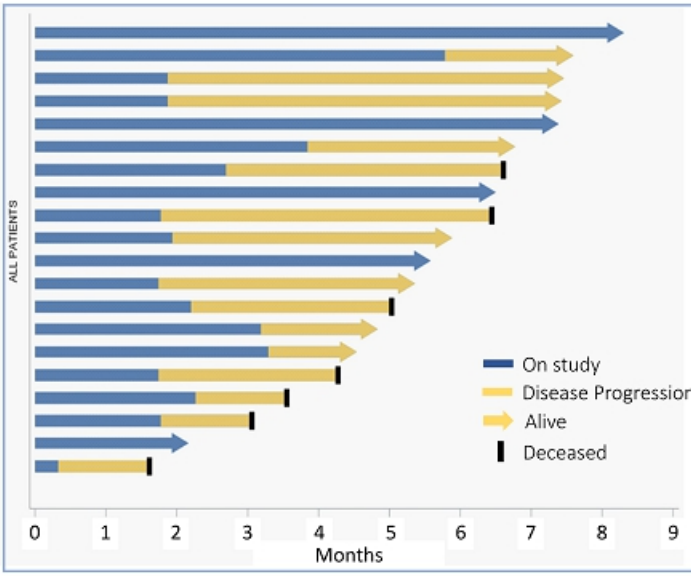
OS is significantly better in patients who experienced dermal injection site reaction, thus supporting the HS-110 mechanism of action

Heat Biologics

# Cohort B:

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

## Duration of Clinical Benefit




5 out of 20 patients have not progressed on therapy

**Median Progression-Free Survival (PFS) 2.7 months**

*As of last data cut-off in April, 2019*

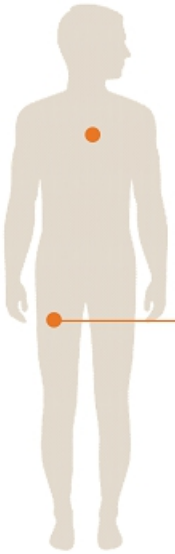
# Safety Profile to Date

*1,000+ Doses - No Serious Adverse Reactions*

## Favorable Safety Profile To Date

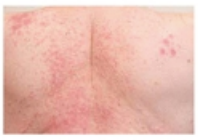
- Over 1,000 doses administered to 120+ patients
- Only one patient ended treatment due to a non-serious adverse reaction*
- No systemic use of steroids required to treat reactions
- No treatment-related serious adverse reactions

**No additive toxicities to standard of care**



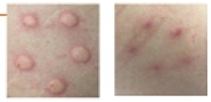
Immune Reaction*

≤ Grade 3 toxicity



Injection Reactions

Week 1 Week 2



*Represents the only patient of ~200 patients dosed who discontinued treatment for a vaccine-related adverse event

# Summary of HS-110 Phase 2 Interim Data

- HS-110 in combination with nivolumab appears safe and well tolerated
- Preliminary results demonstrate the ability of HS-110 plus nivolumab to induce CD8+ T-cell tumor infiltration in previously “cold” tumors
- The occurrence of dermal injection site reactions is associated with improved overall survival in Cohort A
- Data in Cohort B suggests that the addition of HS-110 to nivolumab may restore responsiveness after tumor progression on prior checkpoint inhibitors
- The occurrence of dermal injection site reactions (any grade) is associated with improved progression-free survival and overall survival in Cohort B

# Heat Biologics Acquires Pelican Therapeutics

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

- Heat **acquired 80% controlling interest** in Pelican in May 2017
- Pre-clinical synergy with Heat's *ImPACT®* and checkpoint therapy
- **$15.2M grant award** from the Cancer Prevention Research Institute of Texas (CPRIT) propels PTX-35 through a **~70-patient, first-in-human clinical program**
- PTX-35 is a potential **best-in-class, T-cell co-stimulator** specific to "killer" CD8+ "memory" T-cells

**TNFRSF25 represents an emerging target in immuno-oncology**

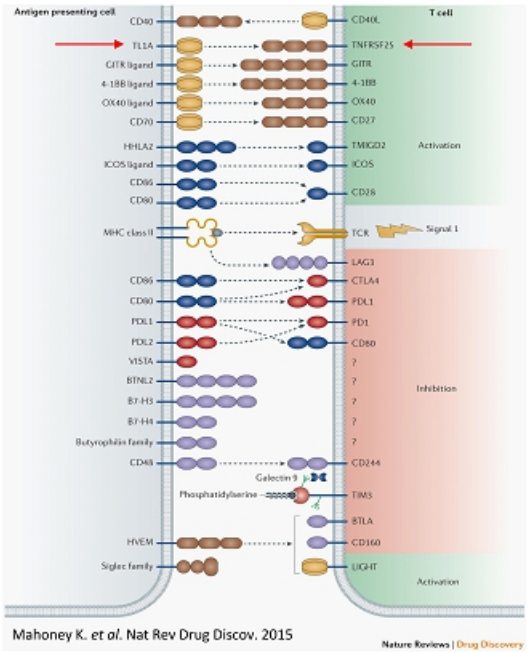
# TNFRSF25 as a Novel I/O Combination Target

- TNFRSF25 is the most recently discovered T cell costimulator, and is a rapidly emerging target

- Pelican is the only company that has publicly announced 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."

*Comments from Gordon Freeman et al*




Mahoney K. *et al.* Nat Rev Drug Discov. 2015

Nature Reviews | Drug Discovery

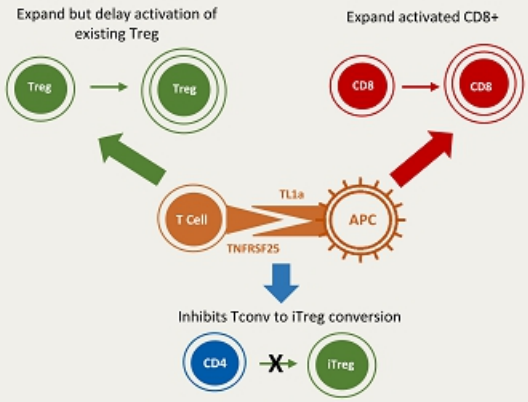
# TNFRSF25: Why So Complicated?

### 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?***

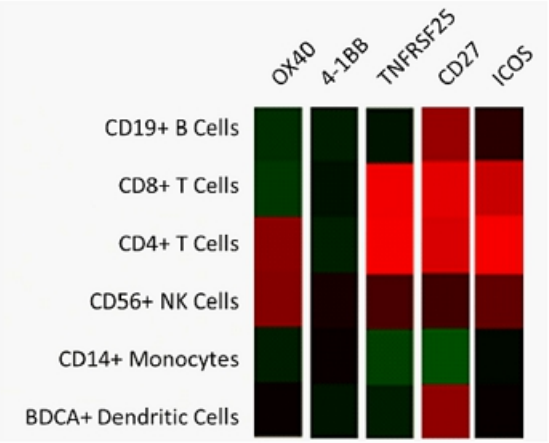
### One molecule – three types of T-cells




***Time and context are everything…***

# TNFRSF25 is Primarily Expressed on CD8+ and CD4+ T-Cells

*compared to other T-cell co-stimulators*




(red = high expression)

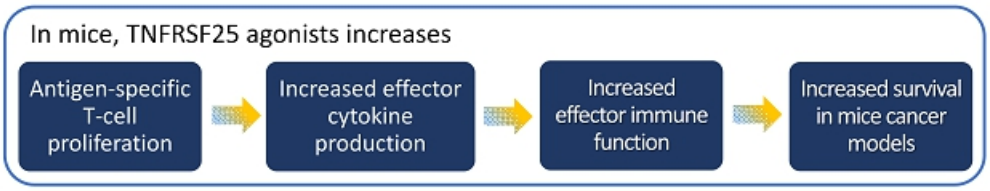
*Genomics Institute of the Novartis Research Foundation* Su *et al.* PNAS 2004:**101**(16);6062-7

# PTX-35 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)

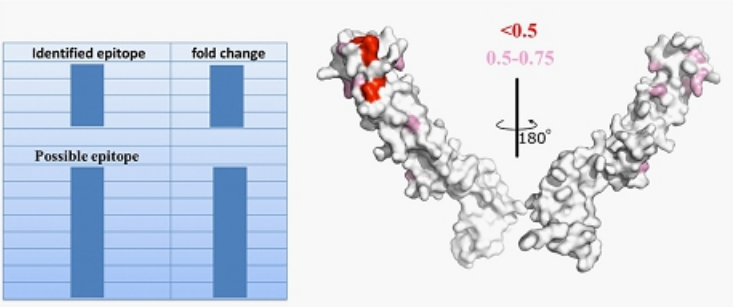



**Compared to agonists OX40, GITR, 4-1BB:**

- TNFRSF25 shows superior activity in stimulating memory CD8+ cells in mice
- TNFRSF25 agonism plus *ImPACT* results in improved survival in mouse melanoma models

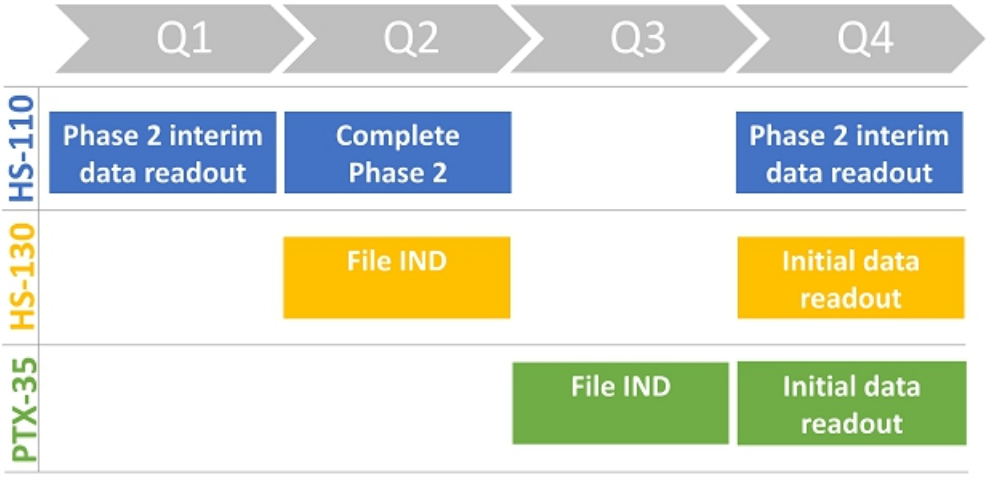
# Development of Agonist Antibody: PTX-35

- The lead mAb, PTX-35, was affinity-matured and selected based on functional activation of TNFRSF25 across species.
- The functional cross-reactivity of PTX-35 was further validated by demonstrating that PTX-35 binds a unique epitope conserved in placental mammals.




- Humanized and affinity matured PTX-35 is now in IND enabling development.
- IND filing slated for Q3 2019.

# 2019 Corporate Milestones



# Corporate Highlights

**Potential Best in Class Oncology Treatment -** T-cell activating platform (TCAP) produces allogeneic, off-the-shelf therapies designed to activate the immune system to turn immunologically "cold" tumors "hot"

**Combination Effect -** Our therapies are designed to be administered with checkpoint inhibitors and other immuno-modulators to enhance immune response

**Off-the-shelf Therapies -** We can administer drug immediately without extracting patient material, simplifying treatment and substantially lowering cost of goods

**Clinical Data with Checkpoint Inhibitors (CPI) -** Positive interim data from ongoing Phase 2 trial of HS-110 + CPI in non-small cell lung cancer (NSCLC) patients (both CPI naïve and CPI progressors)

**Diverse Technology Platforms -** Multiple complementary platform technologies

**Strong Management Team -** Senior team with broad experience in biotech, pharma, clinical development and research

# Appendix

# Management and Advisors

## Management


Jeff Wolf, JD, MBA
Founder & CEO


Jeff Hutchins, PhD
CSO/COO


George Peoples, MD
Chief Medical Advisor


Robert Jacobs
VP of Finance


Lori McDermott, RN, MS
VP of Clinical Dev.


Gary Vinson
VP of Manufacturing

## Scientific Advisors

Robert Levy, Ph.D.
University of Miami

Robert Negrin, MD
Stanford University

Anthony Tolcher, MD
Next Oncology

Roger Cohen, MD
University of Pennsylvania

Llew Keltner, MD, Ph.D.
Epistat

Gary Acton, MD
Advisor

## Board of Directors

Jeff Wolf
Founder, Chairman and CEO

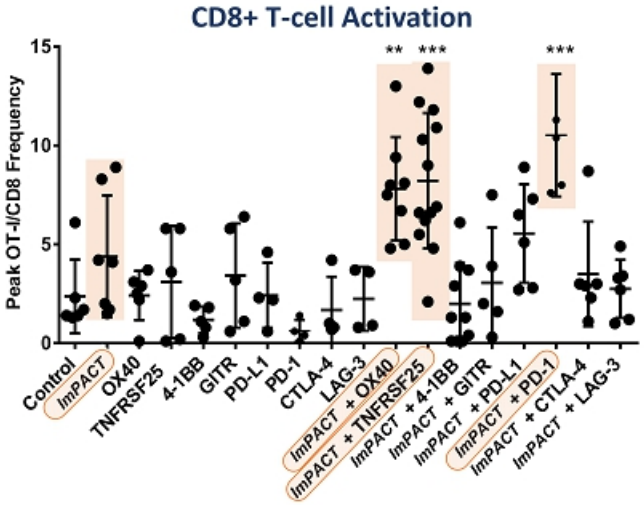
John Prendergast, Ph.D.
Lead Independent Director

John Monahan, Ph.D.
Director

Edward Smith
Director

# Preclinical Data of CD8+ T cell Activation

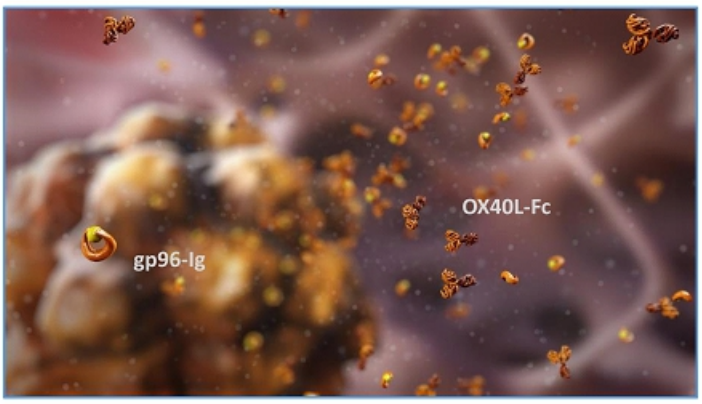
*ImPACT® alone and in combination with co-stimulator agonists: OX40, TNFRSF25, PD-1*




*Source: Fromm et al. Society for Immunotherapy of Cancer Annual Meeting, 2016*

- Higher T-cell responses observed in mice treated with *ImPACT* alone
- *ImPACT®* boosted CD8+ T-cells to even higher levels when combined with co-stimulator agonist antibodies: OX40, TNFRSF25, PD-1
- Findings suggest synergies when combining *ImPACT* with Pelican's TNFRSF25 antibody

# *ComPACT™* Platform Technology

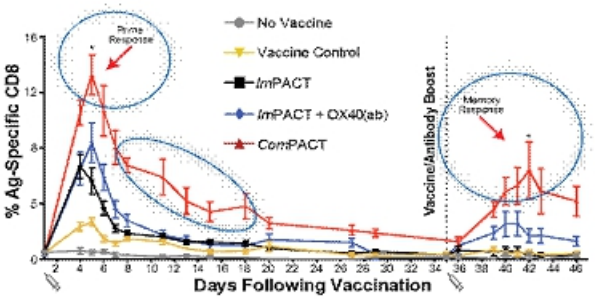



**The first potential dual-acting immunotherapy designed to deliver T-cell activation and co-stimulation in a single product – combination therapy without additive costs**

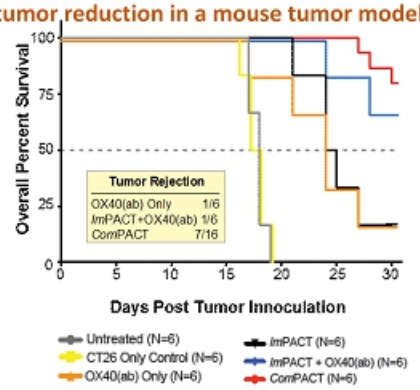
# *ComPACT™* Outperforms OX40

*Monoclonal Antibodies in Pre-clinical Models*

**Superior primary and memory T-cell response in mouse model**




**Translates into increased overall survival and tumor reduction in a mouse tumor model**




***ComPACT* generates ~50% complete tumor rejection compared to ~16% with OX40 agonist antibody combinations**

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

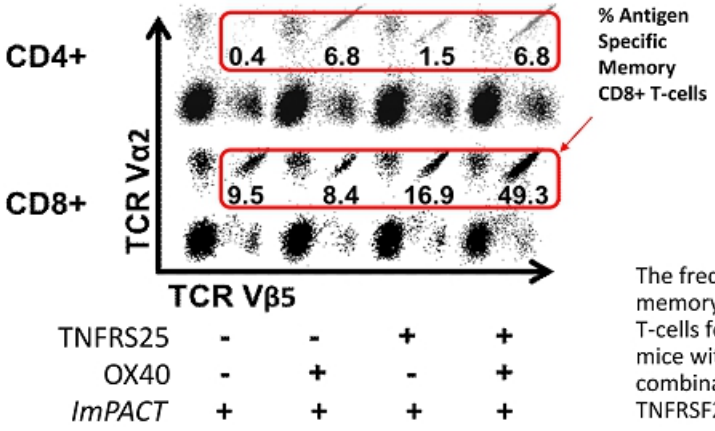
| Target | Companies | Co-stimulator Combinations |
|---|---|---|
| **4-1BB** | Pfizer, ISA Pharma, Gilead, Bristol Myers, Inhibrx, Immatics, Pieris, NCI | **Phase 1/2** Combinations: Chemotherapy, epigenetic modulator, CD20 mAb, HPV vaccine, CART, PD-L1, BTK, Herceptin, modified CD8+ T cells, IL-2, CSF1R, LAG-3, bispecific w/ HER-2, two co-stimulators (w/ OX40) |
| **OX40** | MedImmune, GSK, Incyte, Genentech, Pfizer, AbbVie, Bristol Myers, Alligator Bio | **Phase 1/2** 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 |
| **GITR** | Novartis, Incyte-Agenus, MedImmune, Leap Therapeutics, BMS, OncoMed | **Phase 1** Combinations: PD-1, Fc disabled co-stimulation, hexameric GITR ligand, IDO inhibitor, CTLA-4, GITR ligand-fusion |
| **CD27** | Celldex-BMS, Merck-Aduro | **Phase 1/2** Combinations: PD-1/L-1, sunitinib, CD20, melanoma vaccine, TL3 agonist |
| **ICOS** | Celgene-Jounce, GSK | **Phase 1/2** Combinations: PD-1, CTLA4, docetaxel |
| **TNFRSF25** | Heat (under Pelican) | Filing IND in Q2 2019 in advanced solid tumors. Combination studies being planned |

- 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

# 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***

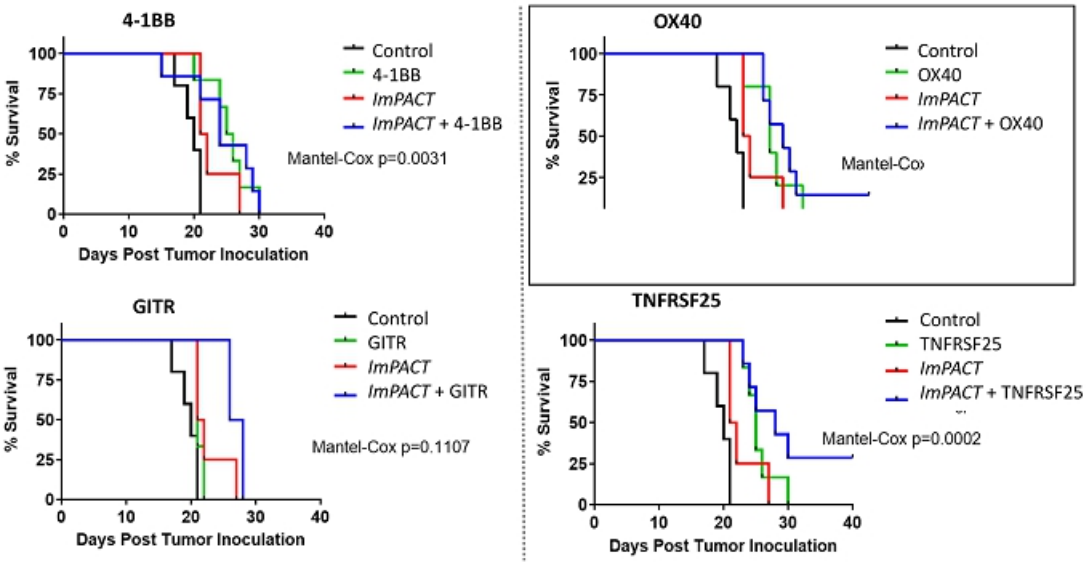



The frequency of antigen-specific memory CD4+ or memory CD8+ T-cells following treatment of mice with *ImPACT™* alone, or in combination with OX40 or TNFRSF25 antibodies

*Schreiber et al. J Immunol 2012:189(7);3311-8*

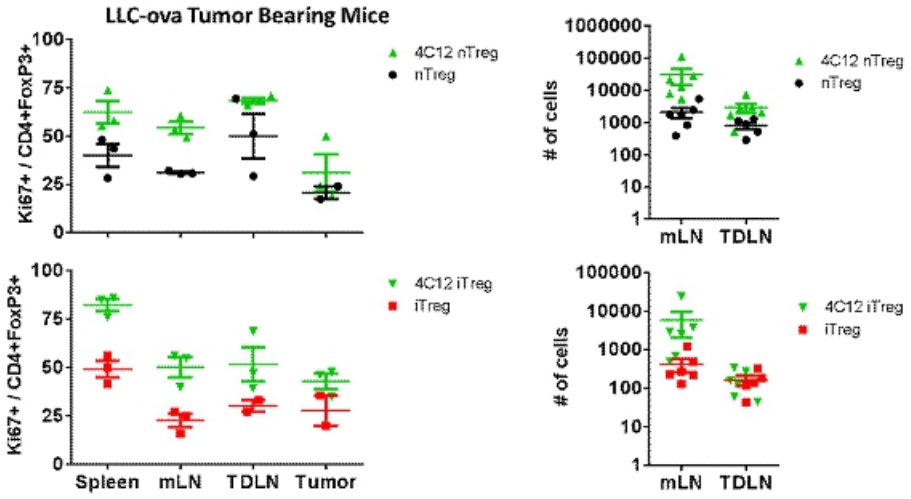
# TNFRSF25 Agonist + ImPACT Significantly Increases Survival

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




*Schreiber T. et al. SITC 2014*

# TNFRSF25 Causes No Intra-tumoral T-reg Proliferation in a Lung Tumor Model




George Fromm et al 2014 Heat Biologics Internal Data