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 2, 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))

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. ☐

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

Item 7.01 Regulation FD Disclosure.

Members of the management team of Heat Biologics, Inc. (the "Company") and certain clinical investigators in itsongoing Phase 2 study investigating HS-110 in combination with Bristol-Myers Squibb's anti-PD-1 checkpoint inhibitor, nivolumab (Opdivo®) presented the information in the presentation poster (the "Poster") entitled "Viagenpumatucel-L (HS-110) plus Nivolumab In Patients With Advanced Non-Small Cell Lung Cancer After Checkpoint Inhibitor Treatment Failure" on June 2, 2019 at the American Society of Clinical Oncology's 2019 Annual Meeting held in Chicago, Illinois. A copy of the Poster is attached to this Current Report on Form 8-K as Exhibit 99.1 and is incorporated herein by reference.

The furnishing of the attached Poster is not an admission as to the materiality of any information therein. The information contained in the Poster is summary information that is intended to be considered in the context of more complete information included in the Company's filings with the Securities and Exchange Commission (the "SEC") and other public announcements that the Company has made and may make from time to time by press release or otherwise. The Company undertakes no duty or obligation to update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases or through other public disclosures.

Item 8.01 Other Events.

On June 3, 2019, the Company issued a press release announcing that on June 2, 2019 members of the management team of the Company and certain clinical investigators in its ongoing Phase 2 study investigating HS-110 in combination with Bristol-Myers Squibb's anti-PD-1 checkpoint inhibitor, nivolumab (Opdivo®) presented the Poster at the American Society of Clinical Oncology's 2019 Annual Meeting held in Chicago, Illinois. A copy of the press release regarding the Poster is attached as Exhibit 99.2 and incorporated herein by reference. The Poster provides new data (including additional interim data and 3 additional months of data since last data release) from the Company's ongoing Phase 2 study investigating HS-110 in combination with Bristol-Myers Squibb's anti-PD-1 checkpoint inhibitor, nivolumab (Opdivo®). The updated results were obtained from Cohort B patients whose data has matured an additional 3 months since last reported at the ASCO-SITC Clinical Immuno-Oncology Symposium in February of this year.

A copy of the Company's new corporate slide presentation that includes information from the Poster is also attached to this Current Report on Form 8-K as Exhibit 99.3 and is incorporated herein by reference.

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

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

The following exhibits are filed with this Current Report on Form 8-K:

Exhibit Number	Description
99.1	Poster presentation entitled "Viagenpumatucel-L (HS-110) plus Nivolumab In Patients With Advanced Non-Small Cell Lung Cancer After Checkpoint Inhibitor Treatment Failure"
99.2	Press Release dated June 3, 2019
99.3	Corporate Presentation dated June 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 3, 2019

HEAT BIOLOGICS, INC.

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

VIAGENPUMATUCEL-L (HS-110) PLUS NIVOLUMAB IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER AFTER CHECKPOINT INHIBITOR TREATMENT FAILURE

Daniel Morgensztern[1], Rachel E Sanborn[2], Lyudmila Bazhenova[3], Saiama N Waqar[1] Lori McDermott[4], Jeff Hutchins[4], David L Rimm[5], Luis E Raez[6], Corey J Langer[7], Roger B. Cohen[7]

[1]Washington University School of Medicine, St. Louis, MO; [2]Earle A Chiles Research Institute, Providence Cancer Institute, Portland, OR; [3]UC San Diego, Moores Cancer Center, San Diego, CA; [4]Heat Biologics, Inc, Durham, NC; [5]Yale School of Medicine, New Haven, CT; [6]Memorial Cancer Institute, Pembroke Pines, FL; [7]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA

Background

Viagenpumatucel-L (HS-110) is an allogeneic cellular immunotherapy that incorporates a broad range of tumor antigens that are known to be shared amongst a high proportion of patients with non-small cell lung cancer (NSCLC). This cell system contains HLA-A1 (a human histocompatibility surface antigen) and gp96-Ig in the form of a transgene constructed from sequences encoding the human gp96 gene with the C-terminal KDEL sequence removed and replaced with the Fc portion of human IgG1. This construct is designed to enable the cell to express the heat shock protein/adjuvant gp96 in secreted form. The secreted gp96 acts as a chaperone to induce cellular immune responses to the tumor antigens expressed by Viagenpumatucel-L (HS-110). gp96 is a unique chaperone because it can activate MHC and up-regulate T-cell co-stimulation and deliver chaperoned antigens to an APC for display via MHC I, with the net result being CD8+ T-cell mediated immune responses[1,2].

The HS110-102 "Durga" Trial is an exploratory, multi-cohort master protocol evaluating HS-110 in combination with anti-PD1 mAbs in the treatment of advanced non-small lung cancer. Here we present interim data from the first twenty patients enrolled in **Cohort B**. This cohort is comprised of previously treated patients with progressive disease (PD) after receiving a minimum of 4 months of checkpoint inhibitor (CPI) therapy at any time prior to study entry. The primary endpoint is objective response rate by RECIST 1.1.

Baseline tissue is collected and tested by Yale Specialized Translational Services Laboratory for tumoral PD-L1 expression (<1% or ≥1%) as well as for CD8+ tumor infiltrating lymphocytes (TILs) within the tumor stroma (≤10% or >10%). Patient subgroups by these tumor characteristics are used in an exploratory analysis to identify potential trends and relationships to clinical outcomes.

Trial ID: NCT02439450

Mechanism of Action

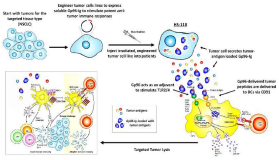

Figure 1: Viagenpumatucel-L (HS-110) Mechanism of Action

HS-110 is derived from the A2100 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. This recognition by APCs results in cross-presentation of antigen to MHC I for the selection of antigen-specific CD8 cells. At the same time, Gp96-Ig binding to TLRs 2 and 4 leads to upregulation of co-stimulatory molecules, which include MHC II and secretion of cytokines and chemokines.

Study Schema

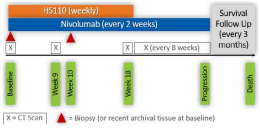

Figure 2: HS110-102 Study Schema

Patients receive weekly HS-110 (1 x 10⁷ cells) intradermally for 18 weeks via 5 simultaneous injections of 0.1ml each, and biweekly nivolumab 240 mg IV until disease progression or unacceptable toxicity

Patient Characteristics

		Cohort B (N = 20)
Median age (range)		65 (56-84)
Female gender		14 (70%)
White race		15 (75%)
ECOG PS 1		10 (50%)
EGFR or ALK positive		2 (10%)
Histology	Adeno Squamous	17 (85%) 3 (15%)
Smoking status	Current/past Never	17 (85%) 3 (15%)
Prior lines of tx	1 2 3 or more	3 (15%) 9 (45%) 8 (40%)
PD-L1	< 1% ≥ 1% Unevaluable	7 (35%) 8 (40%) 5 (25%)
CD8+ TIL	≤ 10% > 10% Unevaluable	7 (35%) 6 (30%) 7 (35%)
Median Time (months) on prior CPI (range)		10.2 (6 – 19)
Median Time (months) between last CPI dose and study entry (range)		1.7 (1 – 21)

Table 1: Patient Characteristics

Baseline patient demographics of Cohort B (n=20).

Objective Response Rate

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

PR	3 (15%)
SD	8 (40%)
Not Evaluable	2 (10%)
DCR	11 (55%)

Tumor shrinkage observed in 35% of patients.

Table 2: Objective Response Rates

ORR for all cohort B patients (n=20) performed locally by site investigators using RECIST 1.1

Overall Survival

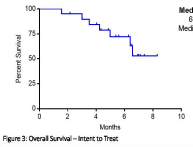

Figure 3: Overall Survival – Intent to Treat

Best Target Lesion Response

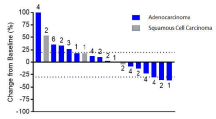

Figure 4: Best Target Lesion Response by Histology and # of Lines of Prior Therapy

Waterfall plot with bar colors representing the histology type. The numerical values presented with each bar indicate the number of lines of prior treatment.

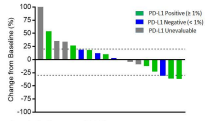

Figure 5: Best Target Lesion Response by PD-L1 Status

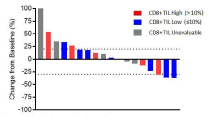

Figure 6: Best Target Lesion Response by TIL Status

Time to Progression

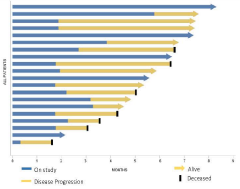

Figure 7: Time to Progression

Swimmer plot showing time until disease progression and current survival status (n=20).

Injection Site Reactions

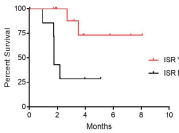

Figure 8: Progression Free Survival

KM plot of patient PFS (n=20) with ISR subgroups (yes or no) shows PFS benefit in patients experiencing at least one injection site reaction (any grade) to HS-110 during study treatment.

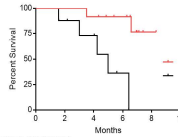

Figure 9: Overall Survival

KM plot of patient OS (n=20) with ISR subgroups (yes or no) shows survival benefit in patients experiencing at least one injection site reaction (any grade) to HS-110 during study treatment.

Frequently Reported Adverse Events

Adverse Events	Cohort B (N=20)
Any Adverse Event	20 (100%)
Fatigue	11 (55%)
Cough	7 (35%)
Dyspnea	7 (35%)
Anemia	4 (20%)
Diarrhea	4 (20%)
Hypocalcemia	4 (20%)
Weight Decrease	4 (20%)
Dizziness	4 (20%)
Headache	4 (20%)
Pruritis	4 (20%)

Table 3: Adverse Event Table

Most commonly reported (>15%) treatment-emergent adverse events (regardless of attribution) occurring in the safety population. There were three Grade 3 events (1 each of embolism, hyponatremia, and pneumonia) and one Grade 4 event (cardiac tamponade), none of which were deemed related to treatment.

Conclusions

HS-110 in combination with nivolumab is well tolerated.

HS-110 in combination with nivolumab demonstrates clinical activity in low CD8+ TIL and PD-L1 negative tumors.

The occurrence of dermal injection site reactions (any grade) is associated with improved progression-free survival and overall survival.

Early data suggest that the addition of HS-110 to nivolumab may restore responsiveness after tumor progression on prior CPI.

References

1. Sribo N, Garcia-Soto A, Schreiber TH, Podack ER. Secreted heat shock protein gp96-Ig: next-generation vaccines for cancer and infectious diseases. Immunologic research 2013;57:311-25.
2. Sribo N, Vaccari M, Pahwa S, et al. Novel vaccination modality provides significant protection against mucosal infection by highly pathogenic SIV. Journal of immunology (Baltimore, Md : 1950) 2013;190:2495-9.

Acknowledgements

The authors are grateful for the investigators, study staff, patients and their families for the commitment to this trial to help advance the treatment of non-small cell lung cancer.

For study-related correspondence, contact lmcdermott@heatbio.com

EXHIBIT 99.2

Heat Biologics Announces Promising Interim Phase 2 Lung Cancer Data Suggesting that HS-110 Plus Nivolumab May Restore Clinical Benefit After Checkpoint Inhibitor Treatment Failure

Clinical benefit observed in 55% of patients receiving HS-110 plus nivolumab after checkpoint inhibitor treatment failure

HS-110 in combination with nivolumab demonstrates clinical activity in low CD8+ TIL "cold tumor" patients and PD-L1 negative tumors

The occurrence of dermal injection site reactions is associated with improved progression free survival (p=0.013) and overall survival (p=0.002)

Cohort B results presented yesterday at the 2019 ASCO Annual Meeting poster session

DURHAM, NC – – June 3, 2019 – Heat Biologics, Inc. (NASDAQ: HTBX), a biopharmaceutical company developing therapies designed to activate a patient's immune system against cancer, today announced compelling new interim results from its ongoing Phase 2 study investigating HS-110 in combination with Bristol-Myers Squibb's anti-PD-1 checkpoint inhibitor, nivolumab (Opdivo®). The updated results were obtained from Cohort B patients whose data has matured an additional 3 months since last reported at the ASCO-SITC Clinical Immuno-Oncology Symposium in February of this year. This data may represent the first Phase 2 data showing clinical activity in non-small cell lung cancer (NSCLC) patients whose disease has progressed after prior treatment with a checkpoint inhibitor (CPI). The Cohort B results were presented yesterday at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting poster session.

COL(ret) George E Peoples, MD, FACS, Heat's Chief Medical Advisor, noted, "These latest Cohort B data provides us even greater confidence that the addition of HS-110 to nivolumab may restore anti-tumor activity in patients whose disease has progressed after treatment with a CPI. Of particular note, 4 out of 5 evaluable patients in Cohort B with PD-L1 negative tumors achieved disease stabilization and 4 out of 7 evaluable patients with low CD8+ TIL levels in their tumors achieved disease stabilization. We are encouraged by these positive results and look forward to reporting additional data later this year."

Jeff Hutchins, Ph.D., Heat's Chief Scientific and Operating Officer said, "The fact that we saw tumor shrinkage in 35% of patients and disease control in 55% of patients whose disease has progressed after treatment with a CPI supports our mechanistic hypothesis that the broad, T-cell mediated immune response activated by HS-110 may improve clinical outcomes for patients who have lost the benefit of treatment with a checkpoint inhibitor. It is also important to note that the occurrence of dermal injection site reactions is associated with statistically significant improved progression free survival and overall survival, providing further support for the mechanism of action of HS-110."

Highlights for Cohort B patients are presented below:

- HS-110 in combination with nivolumab demonstrates clinical activity in 'difficult to treat' low CD8+ TIL (≤10%) and PD-L1 negative (<1%) tumors:
  - 4 out of 5 evaluable patients with PD-L1 negative tumors achieved disease stabilization, 1 of which was a RECIST partial response.
  - 4 out of 7 evaluable patients with low CD8+ TIL tumors achieved disease stabilization, 2 of which were RECIST partial responses.
- The addition of HS-110 to nivolumab may restore clinical benefit to patients whose disease has progressed after CPI treatment failure:
  - Tumor shrinkage observed in 35% of patients
  - Disease control rate of 55%
  - Median Progression-Free Survival (mPFS) of 2.7 months
  - Median Overall Survival (mOS) not yet reached
- The occurrence of any grade dermal Injection Site Reaction during treatment (Y/N) is associated with improved Progression-Free Survival and Overall Survival:
  - mPFS: NR vs 1.8 months; HR 0.17 (95% CI, 0.03-0.84); *p=0.013*
  - mOS: NR vs 5 months; HR 0.13 (95% CI, 0.02-0.71); *p=0.002*

Treatment with HS-110 in combination with nivolumab was well tolerated, with no additional toxicities beyond those observed with single agent CPI therapy.

Trial results are summarized in the official 2019 ASCO Annual Meeting poster.

Trial Design

The Phase 2 trial is designed to evaluate the safety and efficacy of HS-110 combined with an immune checkpoint inhibitor for the treatment of advanced non-small cell lung cancer. Cohort B consists of patients who received a minimum of 4 months of treatment with a checkpoint inhibitor (CPI) as part of their prior therapy, but subsequently had documented progressive disease. Patients receive weekly HS-110 (1×10^7 cells) administered as 5 intradermal 0.1 mL injections for 18 weeks in combination with bi-weekly nivolumab 240 mg IV administered until confirmed disease progression or unacceptable toxicity, whichever occurs first. The primary endpoint is objective response rate (ORR); secondary endpoints include overall survival (OS), progression-free survival (PFS), disease control rate (DCR) and duration of response (DOR). Exploratory endpoints include correlation of clinical outcomes to baseline CD8+ TILs, PD-L1 expression, peripheral blood tumor mutation burden and ELISPOT analysis.

About Heat Biologics, Inc.

Heat Biologics is a biopharmaceutical company developing immunotherapies designed to activate a patient's immune system against cancer using of CD8+ "Killer" T-cells. Our T-Cell Activation Platform ("TCAP") produces therapies designed to turn "cold" tumors "hot" and be administered in combination with checkpoint therapies and other immuno-modulators to increase their effectiveness. HS-110 is our first biologic product candidate in a series of proprietary immunotherapies designed to stimulate a patient's own T-cells to attack cancer. Our *ComPACT* technology is the first potential, dual-acting immunotherapy designed to deliver T-cell activation and co-stimulation in a single product. We are currently enrolling patients in our Phase 2 clinical trial for advanced non-small cell lung cancer, in combination with Bristol-Myers Squibb's nivolumab (Opdivo®) and with Merck's pembrolizumab (Keytruda®). Pelican Therapeutics, Inc., a subsidiary of Heat, is focused on the development of co-stimulatory monoclonal antibody and fusion protein-based therapies designed to activate the immune system. For more information, please visit www.heatbio.com.

Forward Looking Statements

This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 on our current expectations and projections about future events. In some cases, forward-looking statements can be identified by terminology such as "may," "should," "potential," "continue," "expects," "anticipates," "intends," "plans," "believes," "estimates," and similar expressions. These statements are based upon current beliefs, expectation, and assumptions and include statements that the data may represent the first Phase 2 data showing clinical efficacy for non-small cell lung cancer patients whose disease has progressed after treatment with a checkpoint inhibitor (CPI), that the addition of HS-110 to nivolumab may restore anti-tumor activity in patients whose disease has progressed after treatment with a CPI, that the broad, T-cell mediated immune response activated by HS-110 may improve clinical outcomes for patients who have lost the benefit of treatment with a checkpoint inhibitor and the ability of Heat's T-Cell Activation Platform to produce therapies designed to turn "cold" tumors "hot" and to increase their effectiveness of checkpoint therapies and other immuno-modulators. These statements are subject to a number of risks and uncertainties, many of which are difficult to predict, including the ability of Heat's therapies to perform as designed, to demonstrate safety and efficacy, as well as results that are consistent with prior results, the ability to enroll patients and complete the clinical trials on time and achieve desired results and benefits, Heat's ability to obtain regulatory approvals for commercialization of product candidates or to comply with ongoing regulatory requirements, regulatory limitations relating to Heat's ability to promote or commercialize its product candidates for specific indications, acceptance of its product candidates in the marketplace and the successful development, marketing or sale of products, Heat's ability to maintain its license agreements, the continued maintenance and growth of its patent estate, its ability to establish and maintain collaborations, its ability to obtain or maintain the capital or grants necessary to fund its research and development activities, and its ability to retain its key scientists or management personnel, and the other factors described in Heat's filings with the SEC. The information in this release is provided only as of the date of this release, and Heat undertakes no obligation to update any forward-looking statements contained in this release based on new information, future events, or otherwise, except as required by law.

Media and Investor Relations Contact

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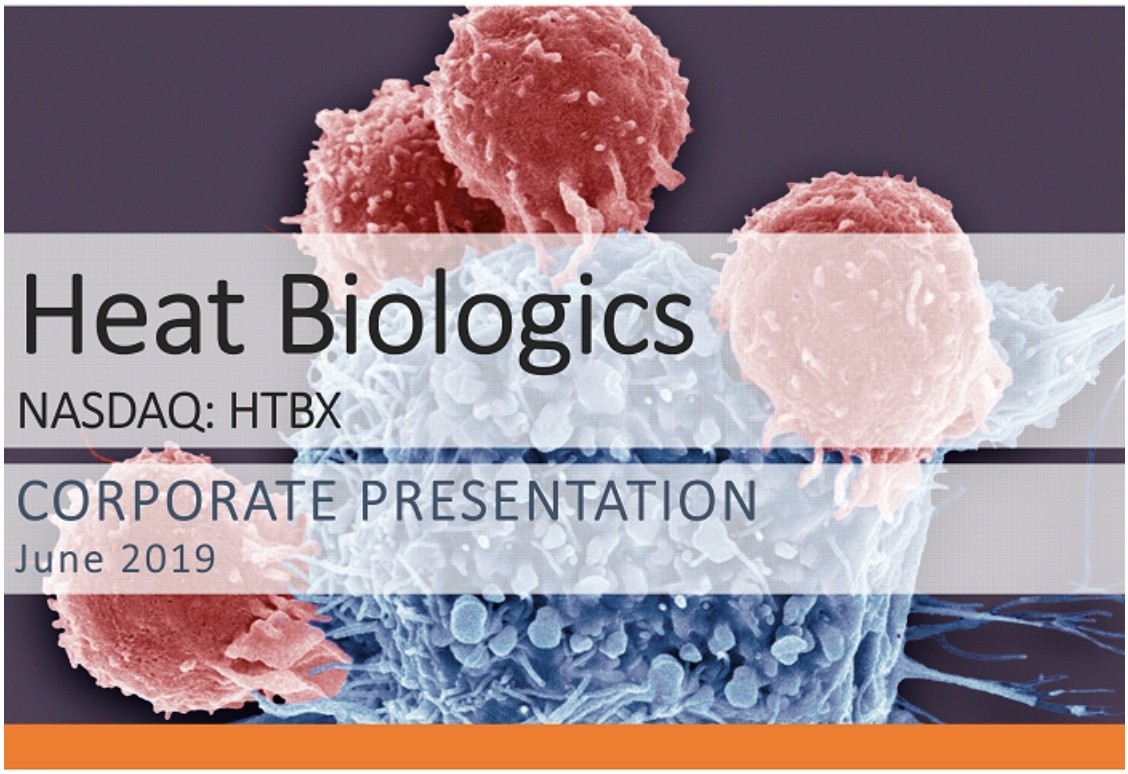

Heat Biologics
Heat Biologics
NASDAQ: HTBX
CORPORATE PRESENTATION
June 2019

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.

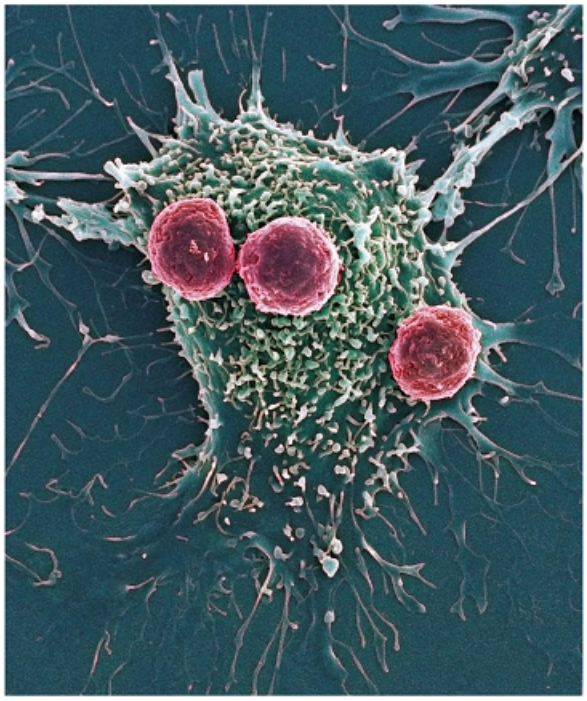
By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines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

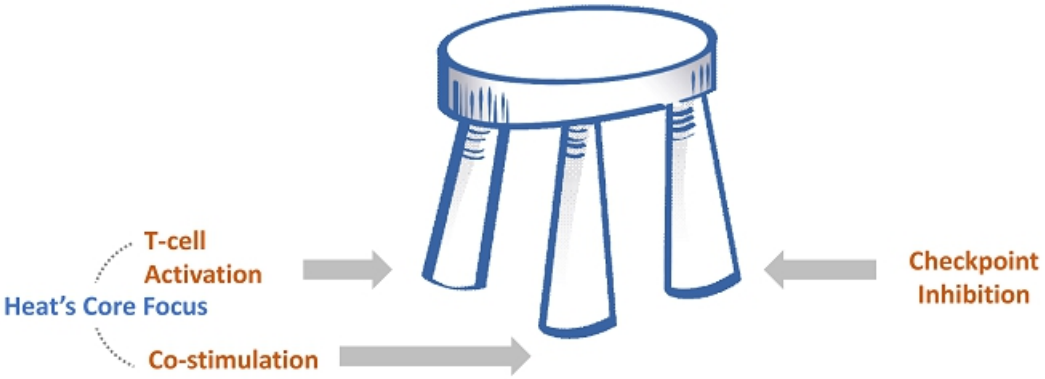
To improve patient outcomes by developing more effective immunotherapies designed to

Turn "COLD" tumors "HOT



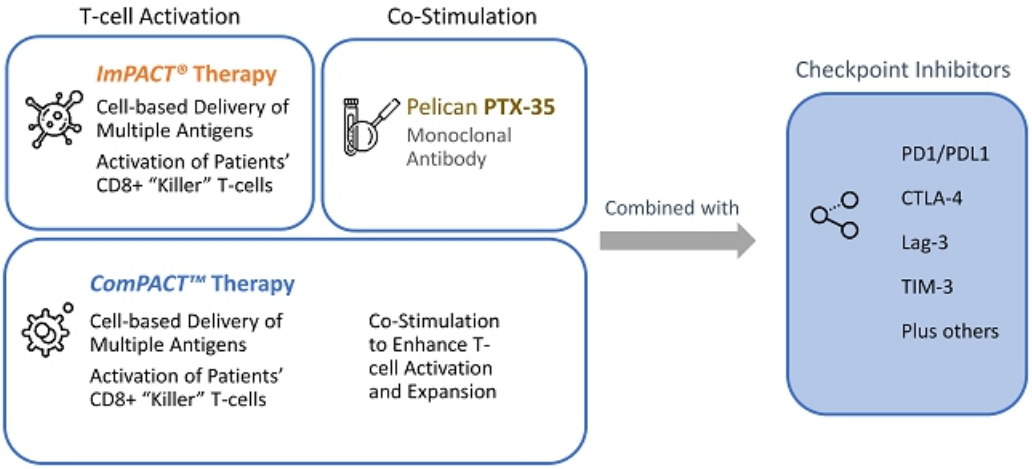
Effective Immuno-Oncology Therapy

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

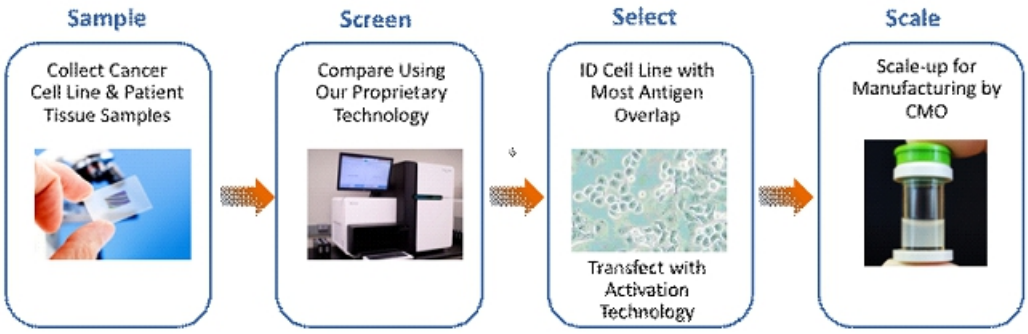
Product Pipeline

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

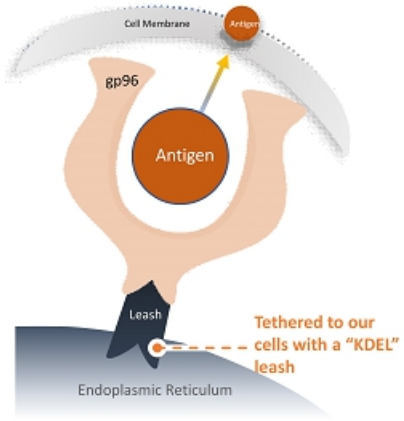


- Frozen, fully-diluted single-dose vial
- Final drug product: 10 million cells
- Easily scaled manufacturing

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

Introducing gp96 – Its dual role

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



"Molecular Warning System"

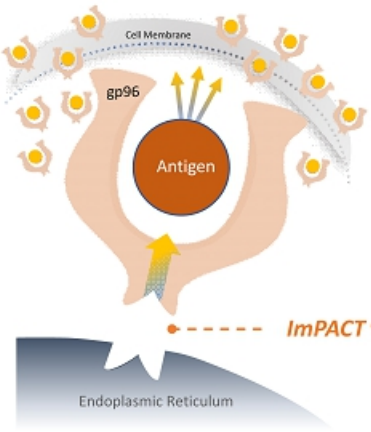
- A natural biological process to deliver proteins (antigens) & gp96 to our immune system
- Gp96 "chaperones" newly-created proteins to the cell membrane where they are released and embedded
- Gp96 chaperoned proteins are only naturally released via necrosis
- Gp96, when present outside the cell, alerts 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



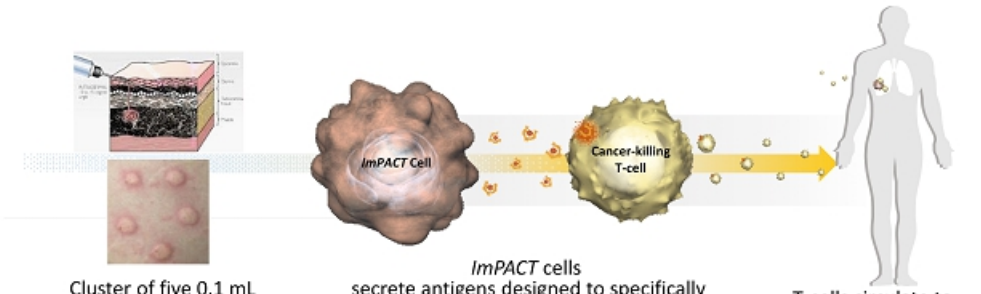
***ImPACT®* technology** genetically modifies tumor cells by "severing the leash" that binds the gp96 to the endoplasmic reticulum, and replacing it with a secretory sequence that pumps gp96 out of the cell

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

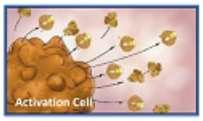
ImPACT®: Immune Pan-antigen Cytotoxic Therapy



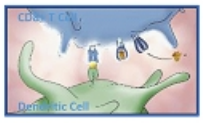
Cluster of five 0.1 mL intradermal injections

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

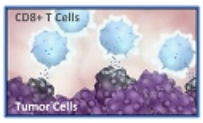
T-cells circulate to destroy patient's tumor



Activated cells **EXPRESS** chaperoned antigens



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



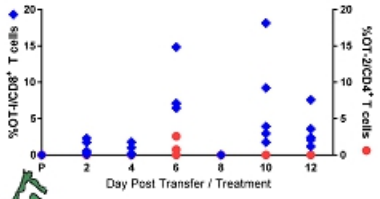
CD8+ T-cells locate and **ELIMINATE** cancer cells

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

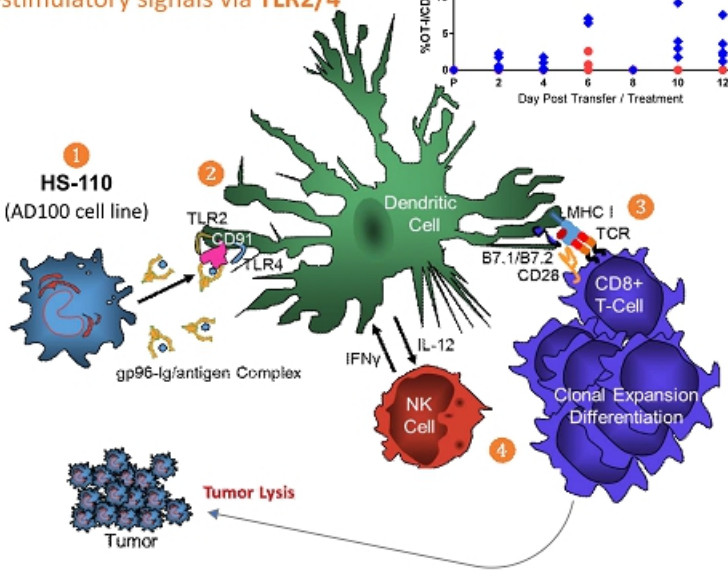
HS-110 Generates an Adaptive Immune Response

2 signals Delivered to APCs:

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



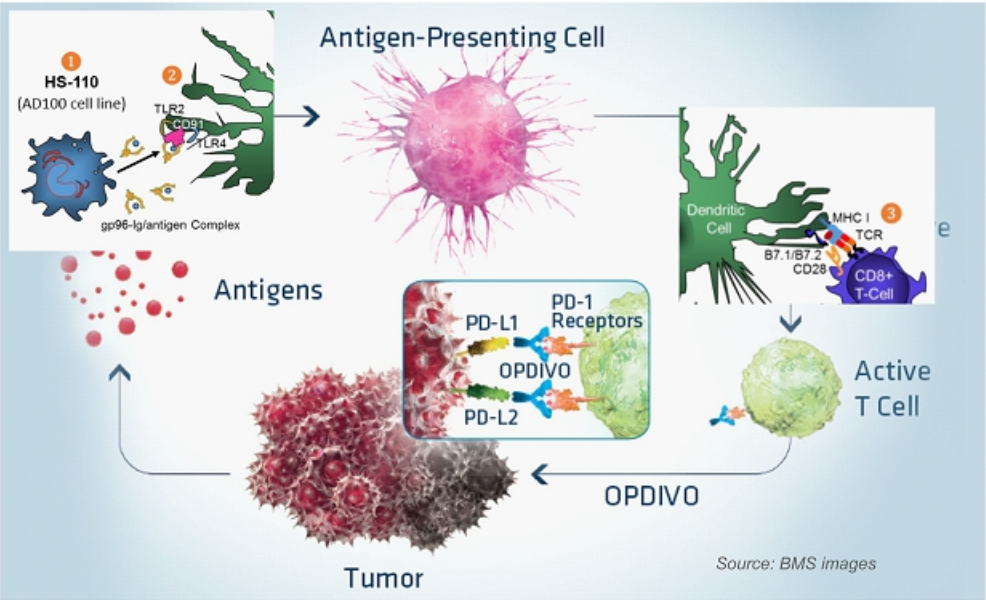
1. **Secretion of gp96-Ig** carrying tumor specific proteins represented on the patients tumor
2. **Activation of APCs** (TLR2/4) and cross-presentation of antigens (CD91)
3. **Specific T-cell receptor** engagement
4. **Clonal Expansion** of Tumor Antigen Specific T cells.



Heat Biologics

HS-110 + Opdivo Combination Therapy

Potential to improve clinical responses and survival, without additional toxicity



Heat Biologics

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**

Heat Biologics

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%)

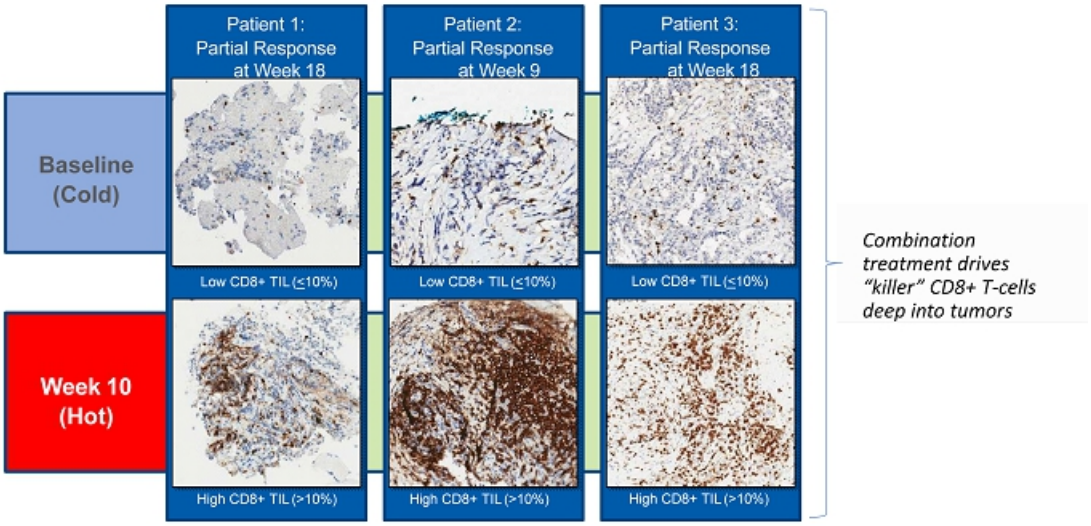
		Cohort A (N = 42)
EGFR or ALK positive		9 (22%)
Prior lines of Tx	1	27 (64%)
	2 or more	13 (30%)
	Unavailable	2 (5%)
PD-L1	< 1%	16 (38%)
	≥ 1%	13 (31%)
	Unevaluable	13 (31%)
CD8+ TIL	≤ 10%	12 (29%)
	> 10%	8 (19%)
	Unevaluable	22 (52%)

As of last data cut-off in January, 2019

Heat Biologics

Clinical Support for HS-110 + Nivolumab Mechanism of Action

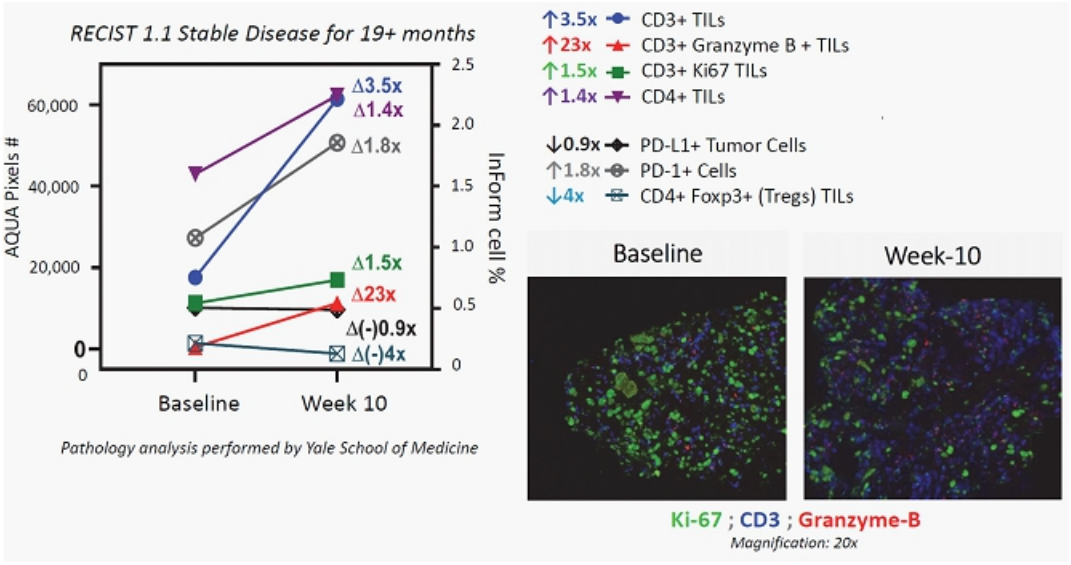
"Turning COLD Tumors HOT"



CD8+ TIL Infiltration Associated with Clinical Response

Heat Biologics

Combination Treatment Substantially Increased Killing Activity in Patient Tumor Microenvironment



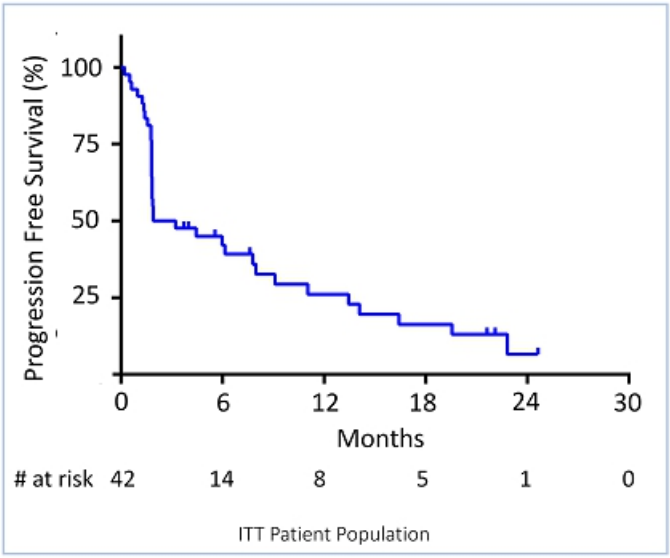
Substantial increase of CD3+ TILs and CD3+ Granzyme B+ TILs for enhanced tumor killing activity

Heat Biologics

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)

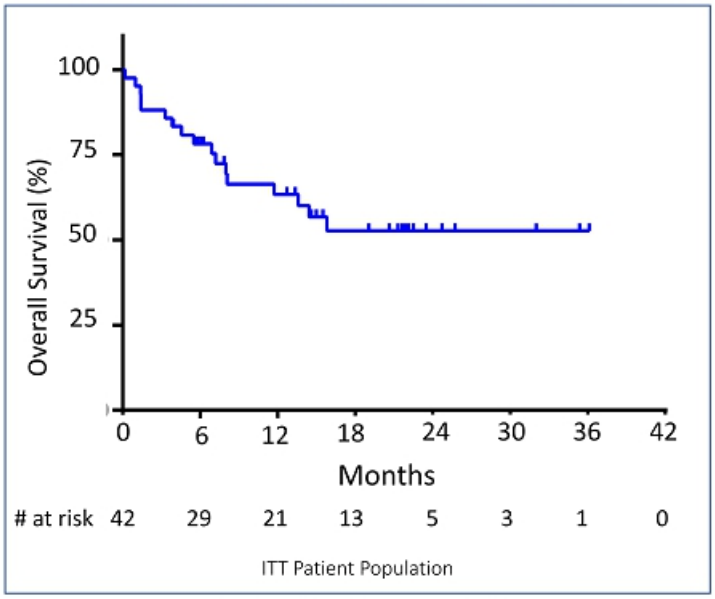
Median PFS of nivolumab alone
2.3 months *
(95% CI: 2.2 – 3.3 months)

* 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*

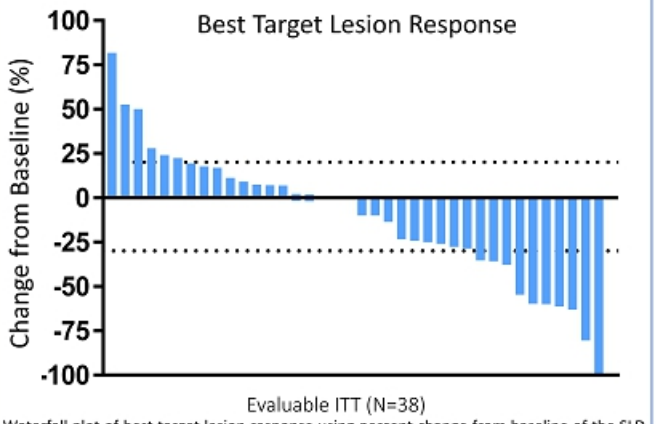
As of last data cut-off in January, 2019

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 had no increase in tumor burden 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%

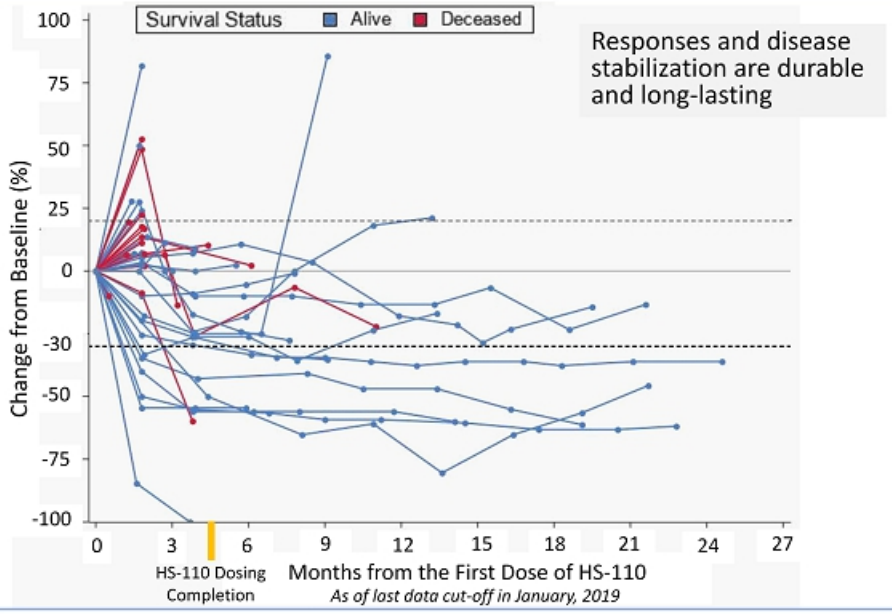
**Borghaei et al 2015 NEJM*

As of last data cut-off in January, 2019

Cohort A:

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

Duration of Benefit



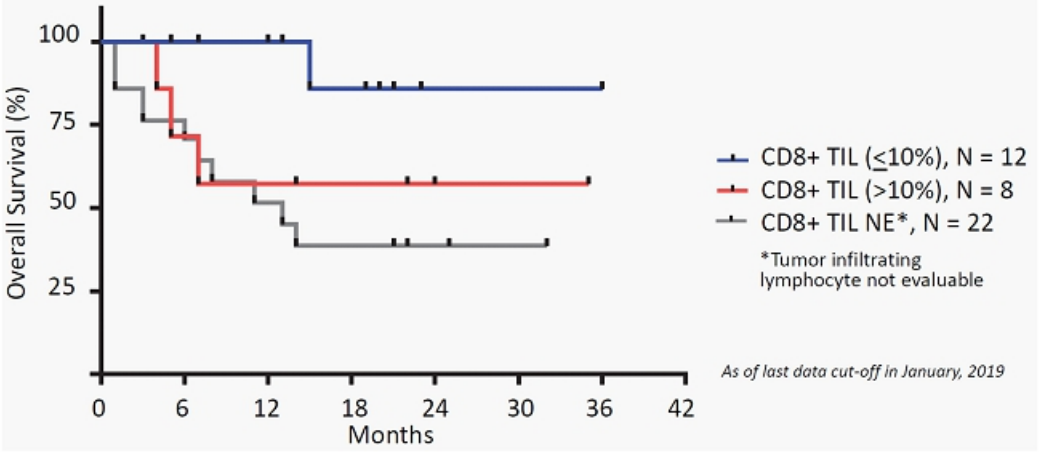
Heat Biologics

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

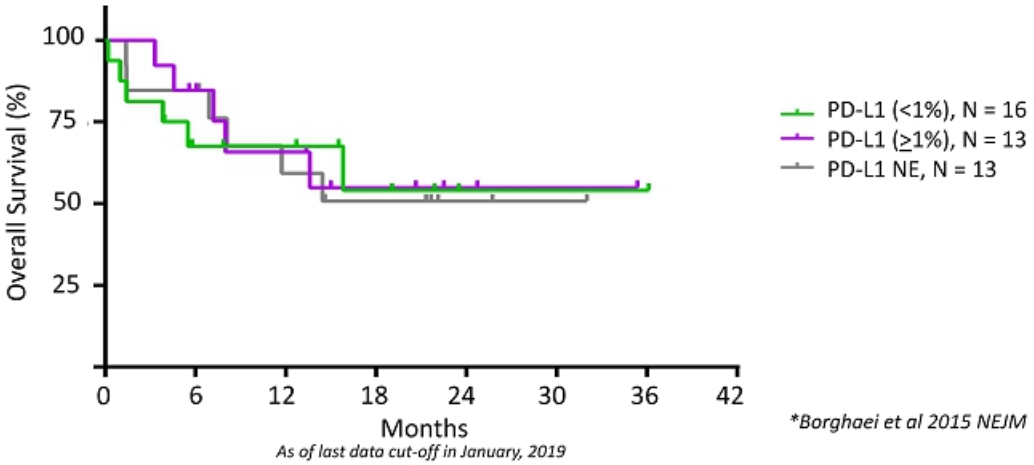
Heat Biologics

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*

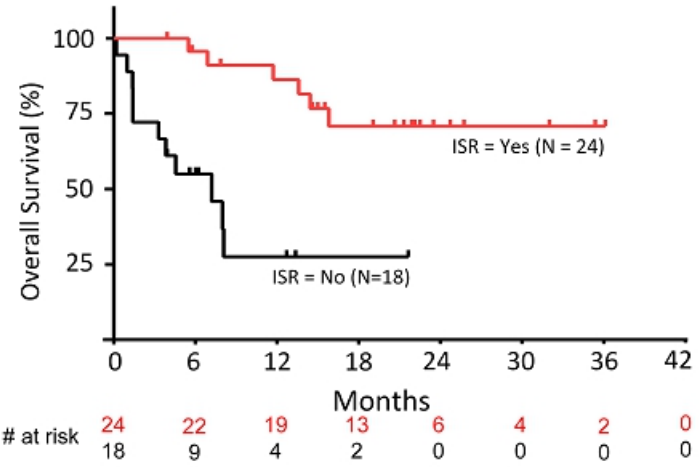
- **Our therapy is agnostic to PD-L1 status**
- Similar survival observed in both PD-L1 positive and PD-L1 negative patients **HR 0.85 (95% CI: 0.26 – 2.79)**
- For nivolumab alone, PD-L1 positive patients typically have better outcomes*

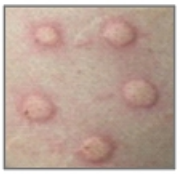
Heat Biologics

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

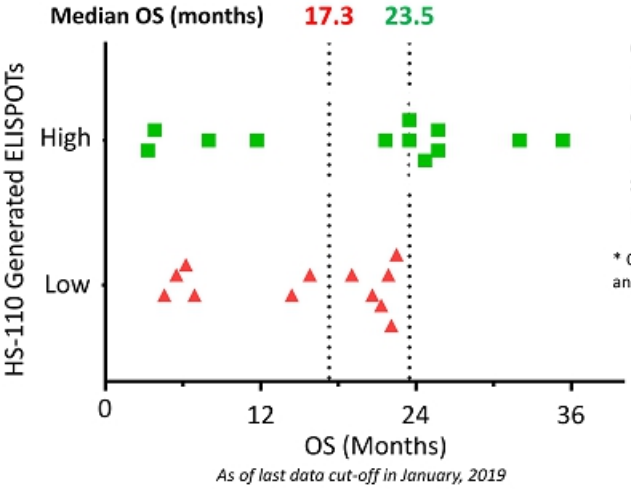
Survival is significantly better in patients who experienced dermal injection site reaction, thus supporting the HS-110 mechanism of action

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%)

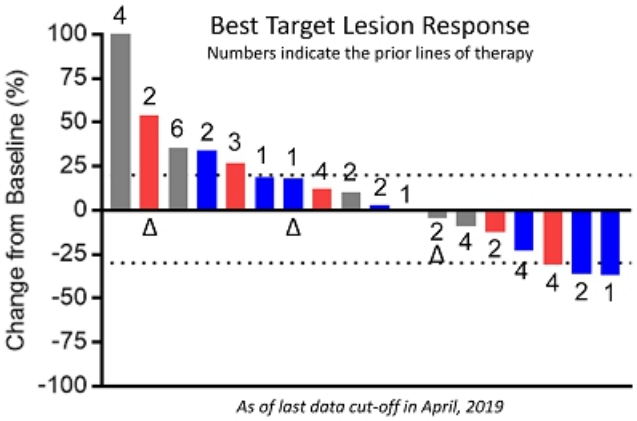
		Cohort B (N = 20)
PD-L1	< 1%	7 (35%)
	≥ 1%	8 (40%)
	Unevaluable	5 (25%)
CD8+ TIL	≤ 10%	7 (35%)
	> 10%	6 (30%)
	Unevaluable	7 (35%)
Time (months) on prior CPI: Median (range)		10.2 (6, 19)
Time (months) between last CPI dose and study entry: Median(range)		1.7 (1, 21)

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

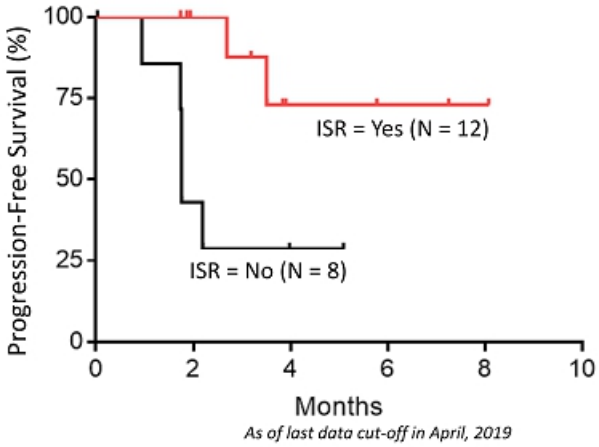
The majority of patients had adenocarcinoma
Δ indicates patients with squamous cell carcinoma

- 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

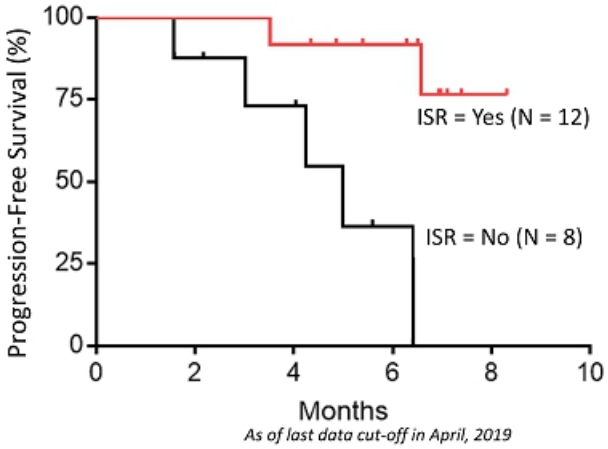
mPFS: NR vs. 1.8 months
HR = 0.17 (95% CI, 0.03-0.84)
p = 0.013

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

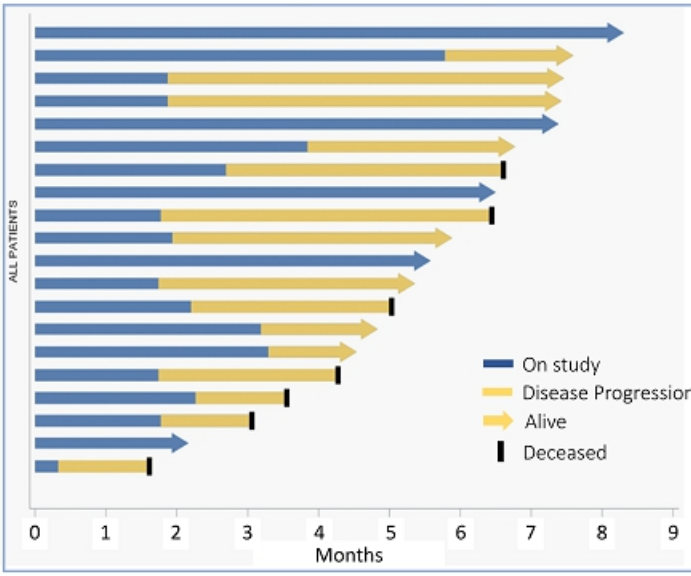
OS is significantly better in patients who experienced dermal injection site reaction, thus supporting the HS-110 mechanism of action

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

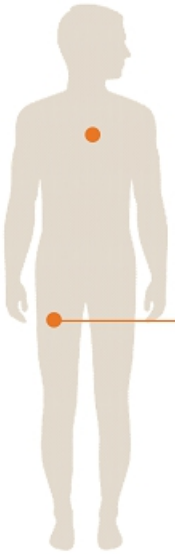
Safety Profile to Date

1,000+ Doses - No Serious Adverse Reactions

Favorable Safety Profile To Date

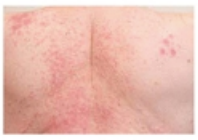
- Over 1,000 doses administered to 120+ patients
- Only one patient ended treatment due to a non-serious adverse reaction*
- No systemic use of steroids required to treat reactions
- No treatment-related serious adverse reactions

No additive toxicities to standard of care



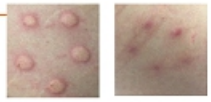
Immune Reaction*

≤ 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

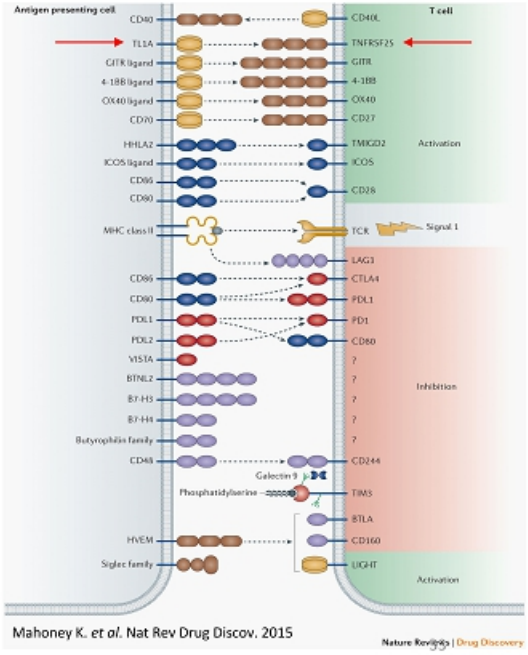
TNFRSF25 as a Novel I/O Combination Target

- 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."

-Gordon Freeman et al



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

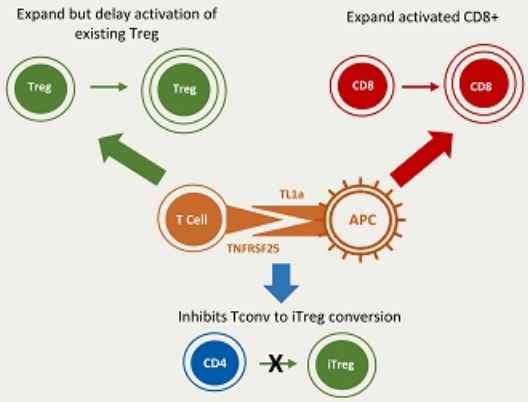
TNFRSF25: Why So Complicated?

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

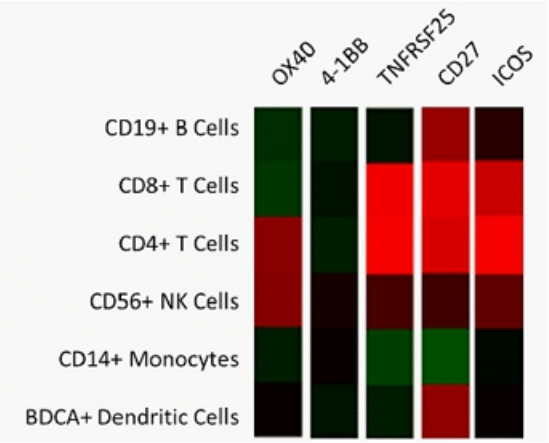


Time and context are everything…

34

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

compared to other T-cell co-stimulators



(red = high expression)

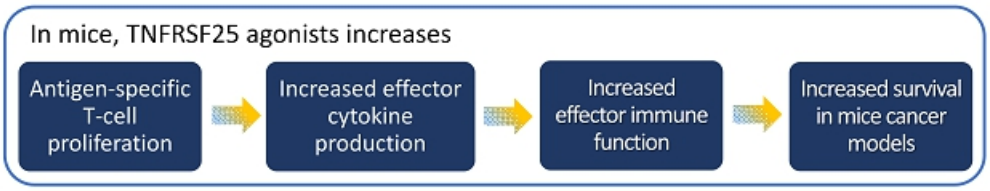
Genomics Institute of the Novartis Research Foundation Su *et al.* PNAS 2004:**101**(16);6062-7

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)



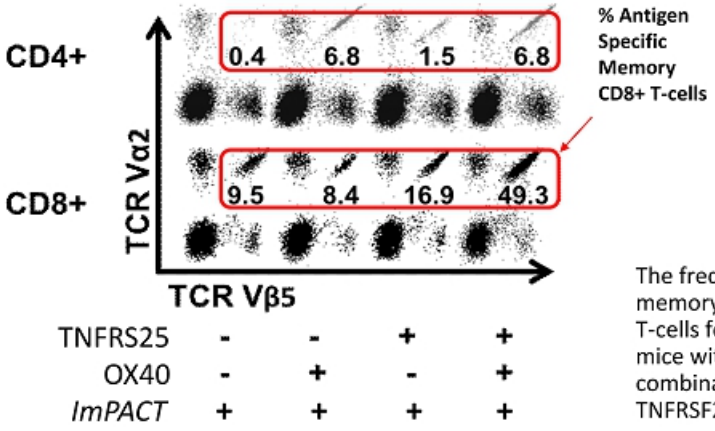
Compared to agonists OX40, GITR, 4-1BB:

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

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

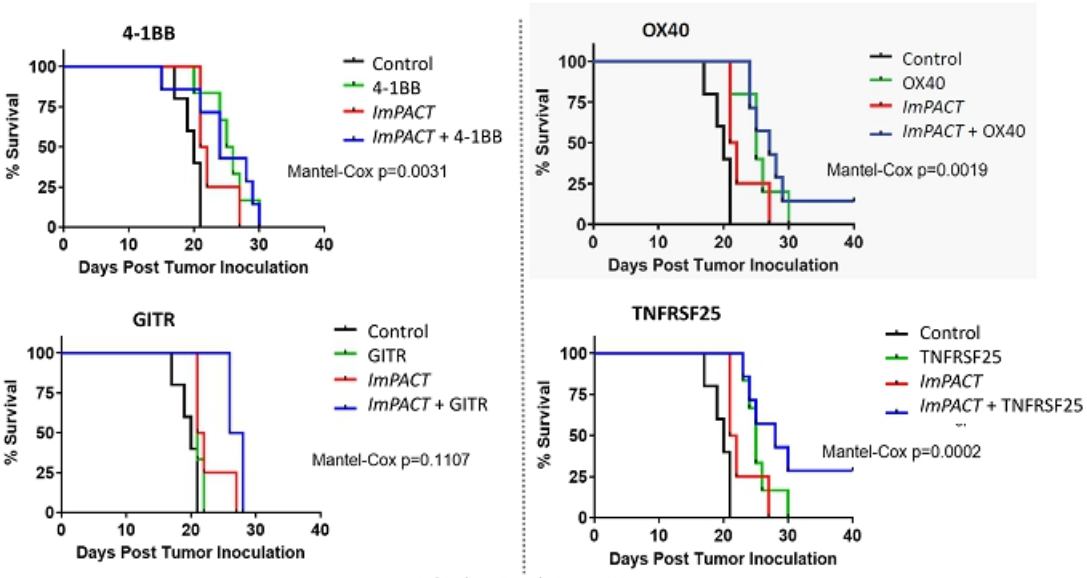


The frequency of antigen-specific memory CD4+ or memory CD8+ T-cells following treatment of mice with *ImPACT™* alone, or in combination with OX40 or TNFRSF25 antibodies

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

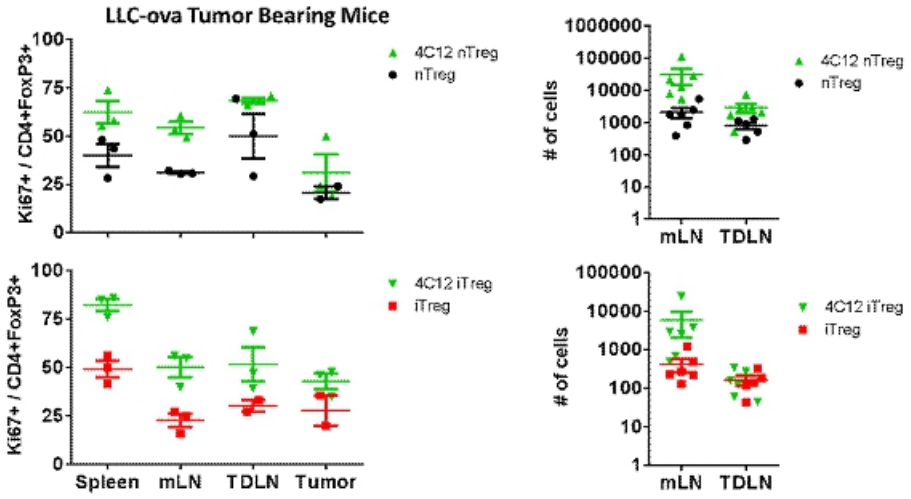
TNFRSF25 Agonist + ImPACT Significantly Increases Survival

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



Schreiber T. et al. SITC 2014

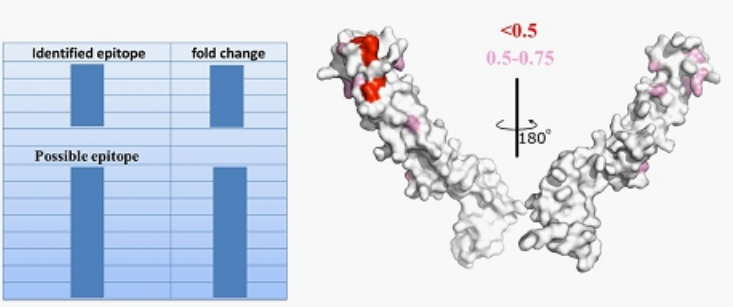
TNFRSF25 Causes No Intra-tumoral T-reg Proliferation in a Lung-tumor Model



Unpublished
George Fromm et al; Heat Biologics, 2014

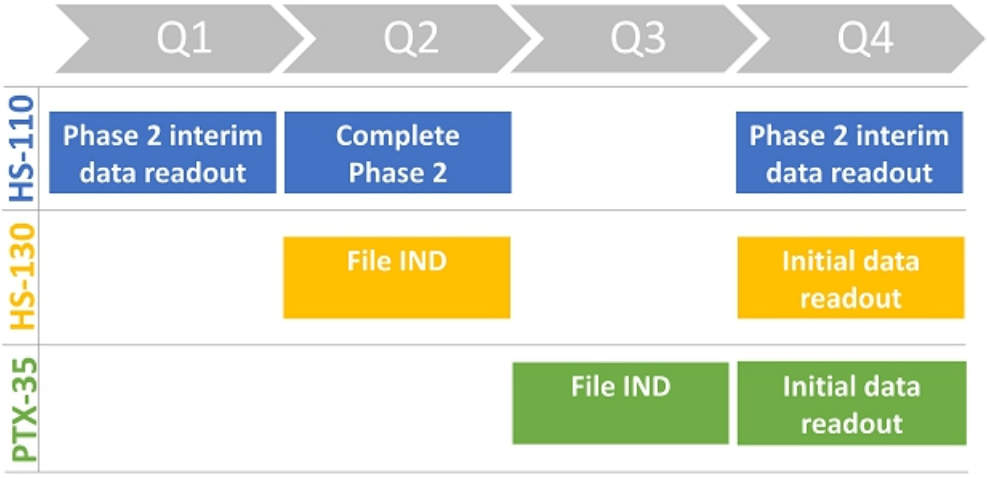
Development of Agonist Antibody: PTX-35

- 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 2Q2019.

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

Heat Biologics

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

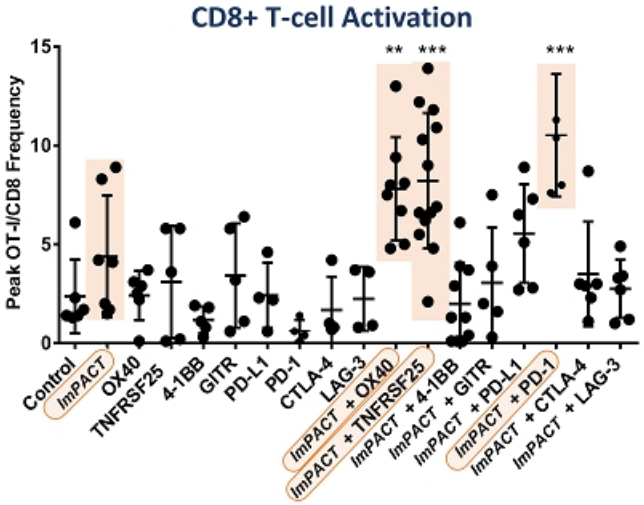
John Prendergast, Ph.D.
Lead Independent Director

John Monahan, Ph.D.
Director

Edward Smith
Director

Preclinical Data of CD8+ T cell Activation

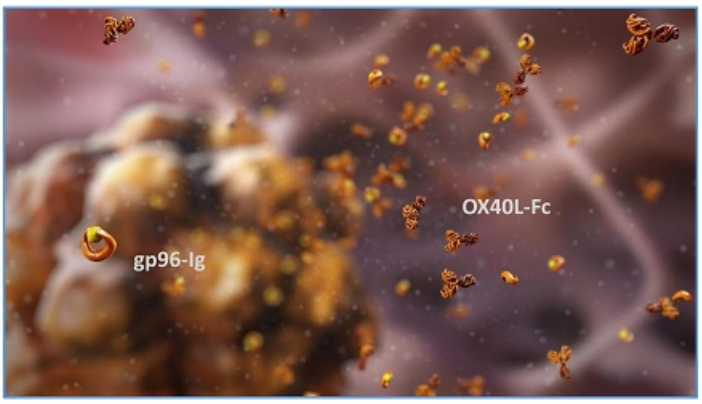
ImPACT® alone and in combination with co-stimulator agonists: OX40, TNFRSF25, PD-1



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

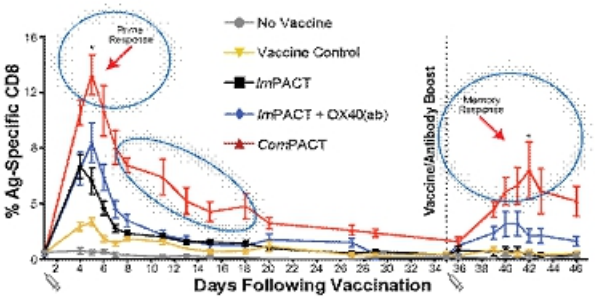


The first potential dual-acting immunotherapy designed to deliver T-cell activation and co-stimulation in a single product – combination therapy without additive costs

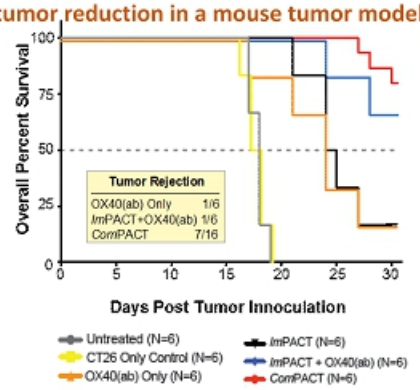
ComPACT™ Outperforms OX40

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