
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): **November 29, 2019**

Heat Biologics, Inc.

(Exact name of registrant as specified in charter)

Delaware

(State or other jurisdiction of incorporation)

001-35994

(Commission File Number)

26-2844103

(IRS Employer Identification No.)

627 Davis Drive

Morrisville, North Carolina 27560

(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(b) 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 slide presentation attached as Exhibit 99.1 hereto, which is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

The following exhibit is being filed as part of this Report.

<u>Exhibit Number</u>	<u>Description</u>
99.1	Presentation materials to be provided at Heat Biologics, Inc. presentations



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: November 29, 2019

HEAT BIOLOGICS, INC.

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



Heat Biologics

NASDAQ: HTBX

CORPORATE PRESENTATION

NOVEMBER 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.

Snapshot of Heat Biologics (Nasdaq: HTBX)

- **Biopharmaceutical company developing a suite of potential first-in-class immunotherapy products**
- **HS-110, an “off the shelf” cell-based immunotherapy product that has the potential to improve PD(L)-1 based therapy**
 - Planning for registrational trial
 - Ongoing Phase 2 program demonstrates signals of efficacy in two treatment settings
 - Broad market potential in multiple oncology indications
 - Fully allogeneic product with low COGs
- **Promising pipeline based on T-cell activation and co-stimulation**
 - IND clearance by US FDA for HS-130, IND clearance for PTX-35 expected in Q2, 2020
 - Product pipeline offers additive clinical benefit when combined with anti-PD-(L)1 and other immunotherapies
- **Experienced management team with proven track record advancing oncology drugs to the market**

Product Pipeline

Product	MOA (Modality)	Indication	Preclinical	Phase 1	Phase 2	Phase 3
HS-110	gp96 (Cell Therapy)	NSCLC				
HS-130	OX40L (Cell Therapy)	Multiple Solid Tumor				
PTX-35	TNFRSF25 (mAb)	Multiple Solid Tumor				

HS-110 Overview

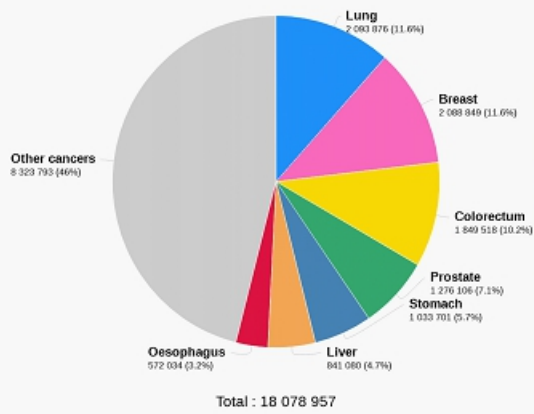
- **HS-110 is a Phase 2 cell-based immunotherapy administered in combination with PD-(L)1 therapies to improve clinical outcomes for NSCLC patients**
 - Allogeneic cells with engineered gp96 to present 70+ different cancer testis antigens
 - Selectively activate CD8+ “killer” T cells
 - gp96 can up-regulate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

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

References: Strbo et al 2013. Immunologic research; Strbo et al 2013. Journal of immunology; Yifei Wang et al. 2018. J Immunol; Heat Biologics Internal data; ‡ Shukuya & Carbone 2016. Journal of Thoracic Oncology, Vol.11 No.7: 976 - 988

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

Estimated Number of New Cases in 2018 Worldwide



Cancer	Cases	
	Number	Percentage
Lung	2 093 876	11.6%
Breast	2 088 849	11.6%
Colorectum	1 849 518	10.2%
Prostate	1 276 106	7.1%
Stomach	1 033 701	5.7%
Liver	841 080	4.7%
Esophagus	572 034	3.2%
Other cancers	8 323 793	46%

PD(L)-1
approved
indications
in US*

* Including
microsatellite
instability-high
cancer

International Agency for Research on Cancer



Heat Biologics

Combination of HS-110 and PD(L)-1 therapy

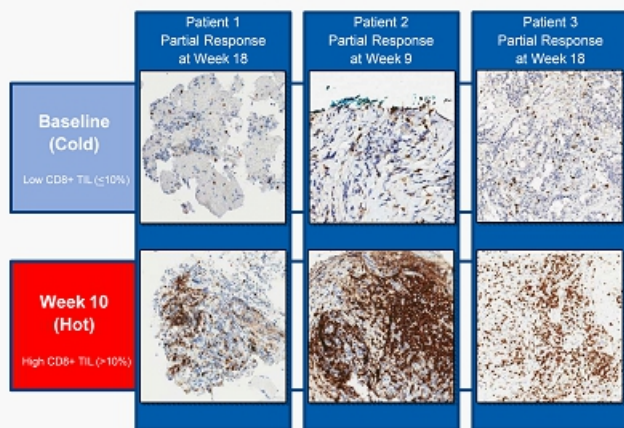
- HS-110 is designed to overcome mechanisms of immune evasion, thereby having the potential to enable effective treatment with PD(L)-1
 - Target to be effective in patients that generally do not benefit from PD(L)-1 therapy



**Pie chart for illustrative purposes and not drawn to scale*

Clinical Support for HS-110 + Nivolumab MOA

“Turning COLD Tumors HOT”



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

CD8+ TIL Infiltration Associated with Clinical Response

Data from Phase 1b/2 trial in advanced NSCLC patients treated by HS-110 + Nivolumab at $\geq 2L$

HS-110 Clinical Data

A Phase 1b/2 Study of HS-110 in Combination with Multiple Treatment Regimens in Patients with NSCLC

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

HS-110 + Nivolumab

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

HS-110 + Pembrolizumab ± Pemetrexed

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

Primary Endpoints

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

Secondary Endpoints

- **OS, PFS, DCR, DOR**

Exploratory Endpoints

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

Cohort A:

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

Trial Result Summary

Compare with Published Data

A comparison with published literature in NSCLC patients treated with *nivolumab as a single agent*

	HS-110 + Nivolumab ^Δ 93% Non-squamous NSCLC 7% Squamous NSCLC	Nivolumab [*] Checkmate 57 Non-squamous NSCLC	Nivolumab [‡] Checkmate 17 Squamous NSCLC
ORR	20%	19%	20%
DCR	46%	44%	49%
Median PFS (months)	1.9	2.3	3.5
Median OS (months)	16.9 50% of pts still alive with median follow-up time of 17 months	12.2	9.2

^Δ Heat Biologics Cohort A interim results as of July 2019 data cut, n=46

^{*} Borghaei et al. 2015 New England Journal of Medicine. 373:1627-39, n=292

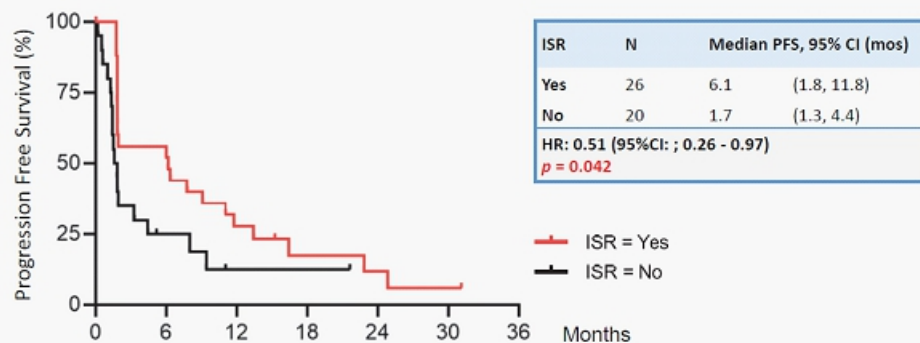
[‡] Brahmer et al. 2015 New England Journal of Medicine. 373:123-135, n=135

Cohort A:

CPI naïve pts treated by
HS-110 + Nivolumab at $\geq 2L$

PFS by Injection Site Reaction (ISR)

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



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

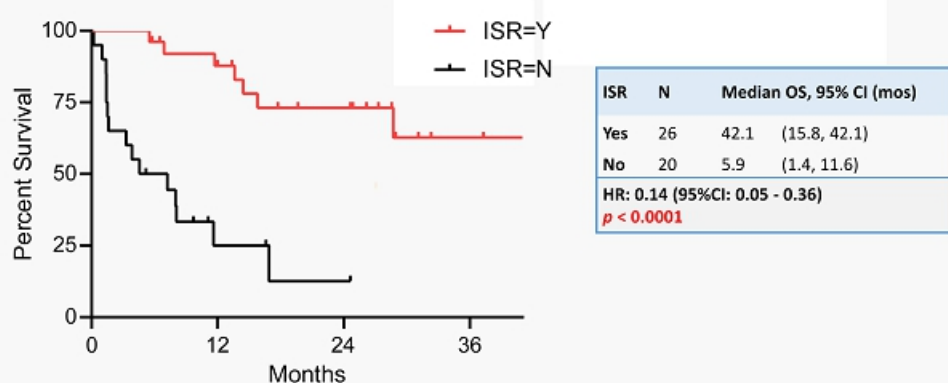
As of July 2019 data cut

Cohort A:

CPI naïve pts treated by
HS-110 + Nivolumab at $\geq 2L$

OS by Injection Site Reaction (ISR)

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



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

As of July 2019 data cut

Cohort A:

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

Summary of PFS and OS

Compare with Published Data

- Cohort A: Stage III or IV advanced NSCLC patients
- A comparison with published literature in NSCLC patients treated with *nivolumab as a single agent*

(Months)	HS-110 + Nivolumab^Δ		Nivolumab	
	93% Non-squamous NSCLC and 7% Squamous NSCLC		Non-Squamous NSCLC	Squamous
	All (n=46)	ISR+ (n=26)	Checkmate 57* (n=292)	Checkmate 17† (n=135)
Median PFS	1.9	6.1	2.3	3.5
Median OS	16.9 50% of pts still alive with median follow-up time of 17 months	42.1	12.2	9.2

^Δ Heat Biologics Cohort A interim results as of July 2019 data cut. Subgroup analysis by ISR was retrospective.

[†] ISR = injection site reaction. [‡] CD8+ TIL = CD8+ tumor infiltration lymphocytes at baseline (High > 10%, Low ≤ 10%). [§] PD-L1 (Positive ≥ 1%, Negative < 1%). NR = Not reached. As of last data cut-off in July, 2019. Median follow-up time = 14.4 months.

HS-110 Clinical Data

A Phase 1b/2 Study of HS-110 in Combination with Multiple Treatment Regimens in Patients with NSCLC

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

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- Cohort C & D: **PFS**

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(Negative defined as $< 1\%$ on tumor cells)
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(Low defined as < 10 mutations/ Mb)
- **ELISPOT cytokine analysis**

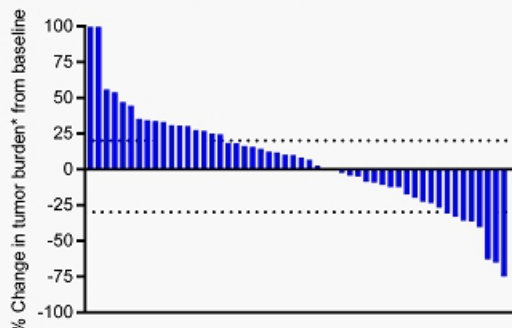
Cohort B:

CPI progressors treated by
HS-110 + Nivolumab at $\geq 2L$

Response and Disease Control

Comparison with Published Data

Tumor shrinkage observed in 38% of patients



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

	HS-110 + Nivolumab ^Δ		Nivolumab [†]
	iRECIST	RECIST 1.1	RECIST 1.1
ORR	14% (8)	13% (7)	8.3% (10)
PR	14% (8)	13% (7)	8.3% (10)
SD	46% (26)	46% (26)	Not Available
Not Evaluable	7% (4)	7% (4)	Not Available
DCR	61% (34)	59% (33)	Not Available

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

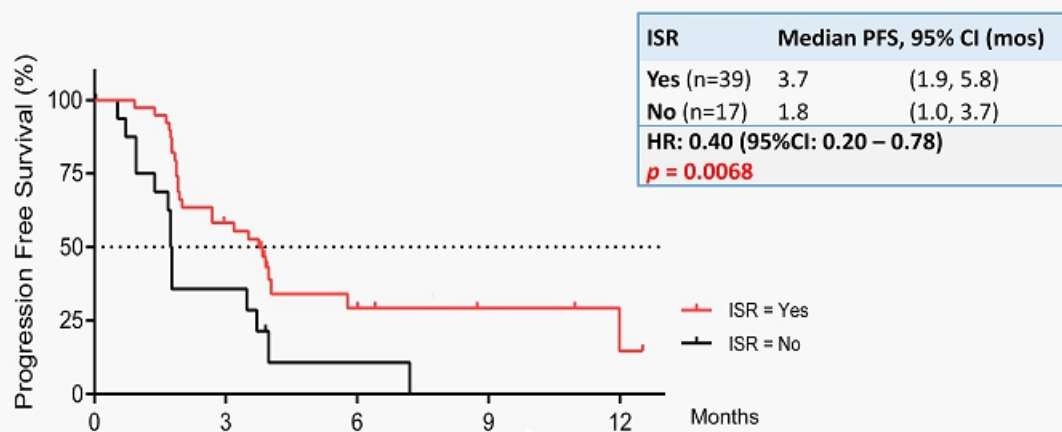
[†] Kazandjian et al 2017 Seminars in Oncology 44(2017)3–7. Retrospective analysis. Two of the 10 patients had unconfirmed responses. N=121.

As of July 2019 data cut

Cohort B:

CPI progressors treated by
HS-110 + Nivolumab at $\geq 2L$

PFS by Injection Site Reaction (ISR)

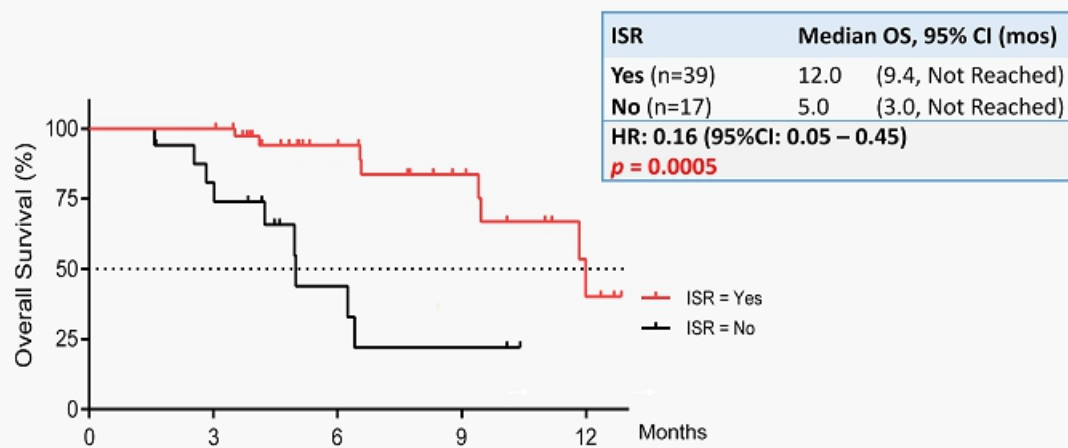


ISR = Yes refers to patients who experienced at least one injection site reaction at any time during treatment (N = 39)

Cohort B:

CPI progressors treated by
HS-110 + Nivolumab at $\geq 2L$

OS by Injection Site Reaction (ISR)



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

As of July 2019 data cut

Cohort B:

CPI progressors treated by
HS-110 + Nivolumab at $\geq 2L$

Summary of PFS and OS

Compared with Published Data

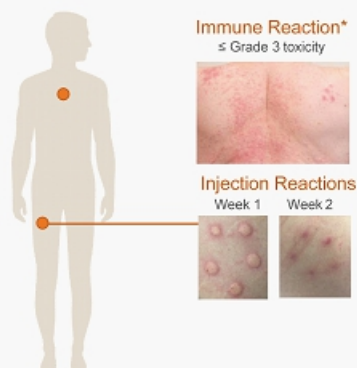
- Unresectable or metastatic NSCLC patients, heavily pretreated (63% with ≥ 2 lines of prior therapy)
- A comparison with published literature in NSCLC patients after PD-(L)1 progression

(Months)	HS-110 + Nivolumab at ≥ 2 nd line after CPI failure Δ		Treatment Options at ≥ 3 rd line after CPI failure		
	All (n=56)	ISR+ (n=39)	Gemcitabine \dagger (n=27)	Docetaxel \dagger (n=25)	Chemotherapy \ddagger (n=28)
Median PFS	3.2	3.7	2.8	2.7	4.7
Median OS	11.8	12.0	7.5	6.8	9.0

Δ Heat Biologics Cohort B as of July 2019 data cut estimate with 70% of the patients still alive. ORR and DCR unconfirmed as study is actively ongoing at time of analyses. ORR performed locally by study Investigators using RECIST 1.1.

\dagger Single agent chemotherapy, Constatini et al 2018 ERJ Open Research \ddagger Schwartzman et al 2017 Lung Cancer

Favorable Safety Profile to Date






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

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

No additive toxicities to standard of care




Product Pipeline

Product	MOA (Modality)	Indication	Preclinical	Phase 1	Phase 2	Phase 3
HS-110	gp96 (Cell Therapy)	NSCLC				
HS-130	OX40L (Cell Therapy)	Multiple Solid Tumor				
PTX-35	TNFRSF25 (mAb)	Multiple Solid Tumor				

HS-130 Overview

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

Product Pipeline

Product	MOA (Modality)	Indication	Preclinical	Phase 1	Phase 2	Phase 3
HS-110	gp96 (Cell Therapy)	NSCLC				
HS-130	OX40L (Cell Therapy)	Multiple Solid Tumor				
PTX-35	TNFRSF25 (mAb)	Multiple Solid Tumor				

PTX-35 Overview

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

Heat Biologics

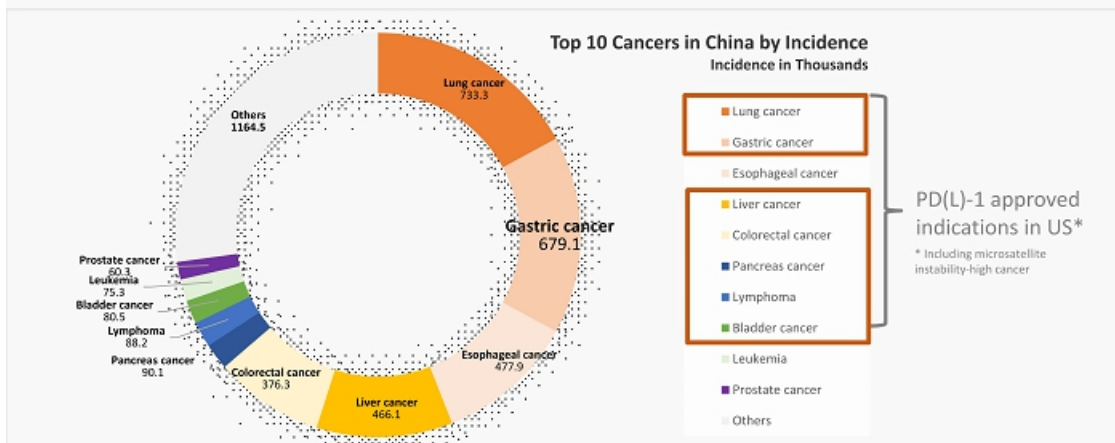
NASDAQ: HTBX

APPENDIX

HS-110

MOA AND PRECLINICAL DATA

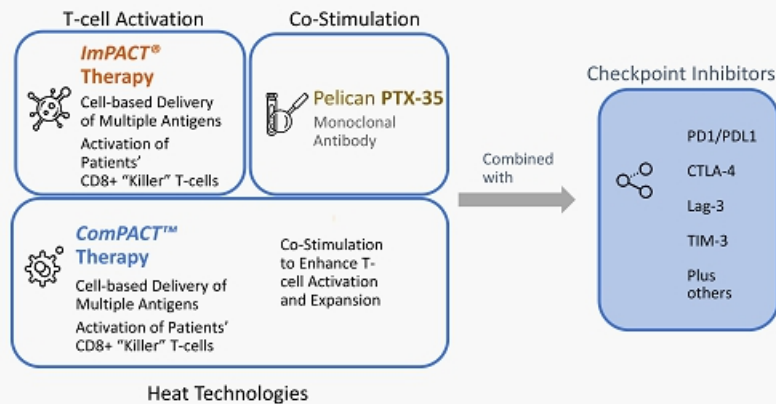
PD(L)-1 Therapy is Approved for Multiple Cancers



Chen et al. 2016 CA Cancer J Clin 66: 115-132

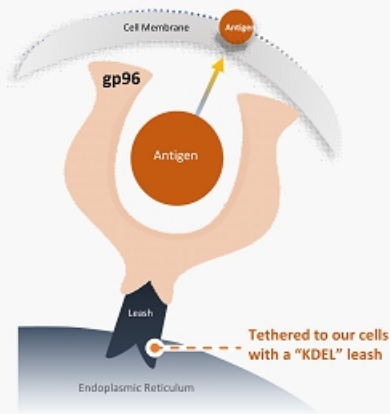
Heat's Combination Platforms

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



Introducing gp96 – Its dual role

The Immune System's "Swiss Army Knife"*



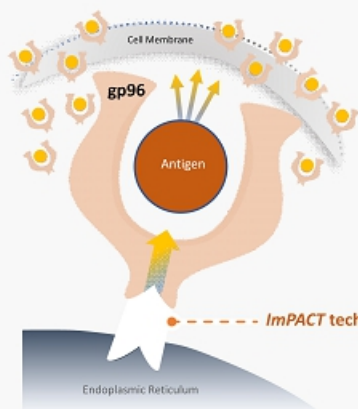
"Molecular Warning System"

- 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"



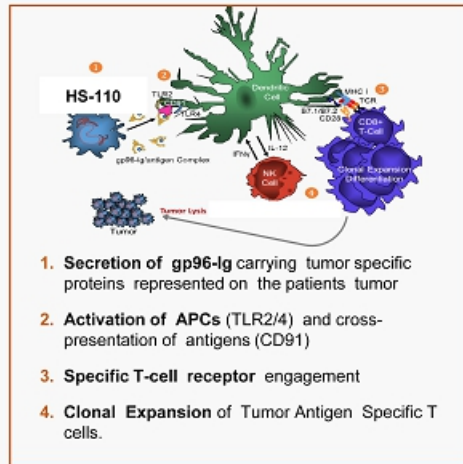
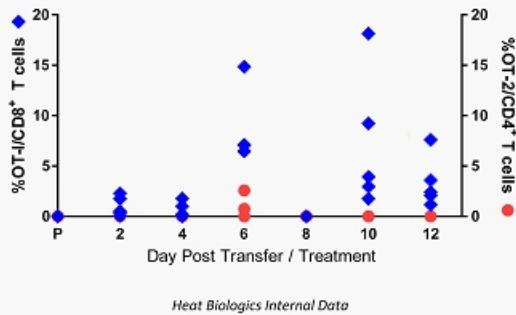
Heat Biologics ImPACT® technology reprograms cancer cells to continuously secrete their own antigens

- **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

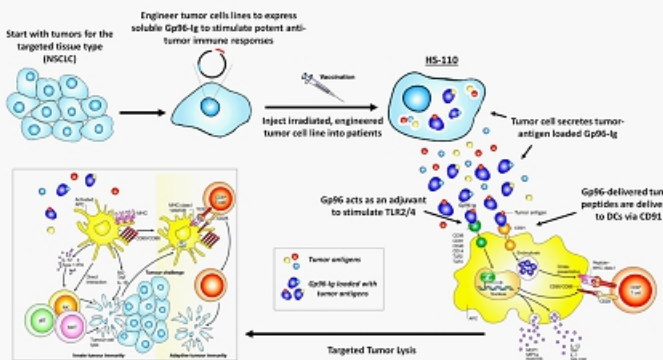
HS-110 Mechanism of Action

2 signals delivered to APCs:

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



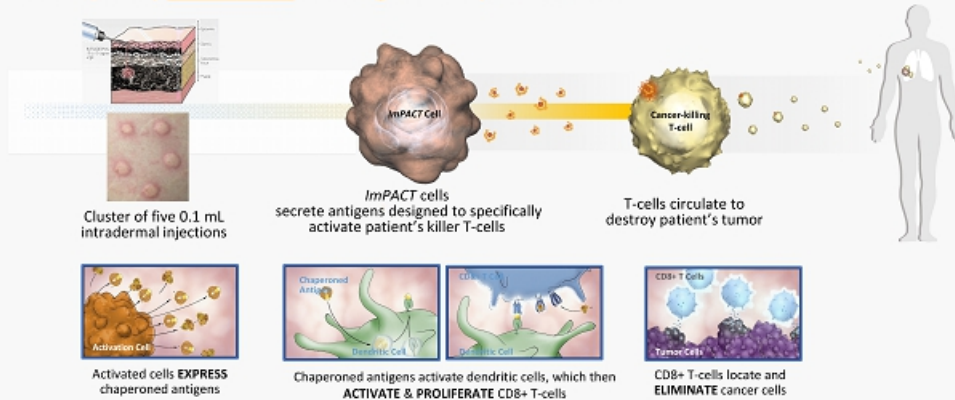
HS-110 Mechanism of Action



- HS-110 is derived from a lung adenocarcinoma cell line transfected with gp96-Ig, where the gp96 KDEL ER retention sequence is replaced by IgG1 Fc
- gp96-Ig acts as a chaperone protein for tumor associated antigens and is recognized by CD91 on APCs; resulting in cross-presentation of antigen to MHC I for the selection of antigen-specific CD8 cells
- gp96-Ig also binds to TLRs 2 and 4 leading to upregulation of co-stimulatory molecules, which include MHC II and secretion of cytokines and chemokines

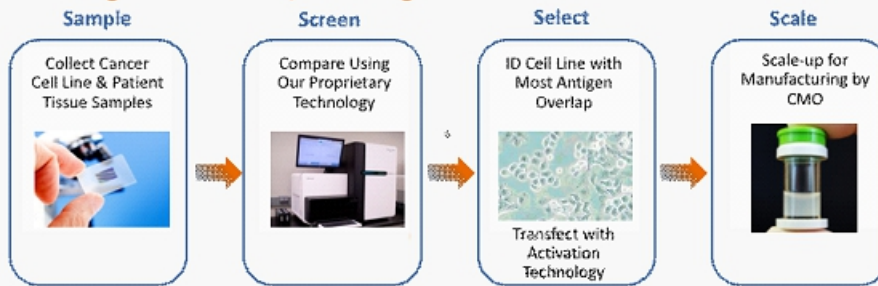
HS-110: Heat's Proprietary Cell Line

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



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**

Cohort B:

*CPI progressors treated by
HS-110 + Nivolumab at $\geq 2L$*

Key Data Summary

- Response rate by RECIST 1.1
 - Objective response rate (ORR) was 13%
 - Disease control rate (DCR) was 59%
- Median overall survival (OS) was estimated at 11.8 months with 70% of patients still alive
- Median progression free survival (mPFS) was 3.2 months
- Patients who experienced an ISR vs. those who did not:
 - Improved PFS (HR = 0.40, p = 0.0068)
 - Improved OS (HR = 0.16, p = 0.0005)
- The effect of HS-110 in combination with nivolumab is not dependent on PD-L1 expression
- Combination of HS-110 and nivolumab was well tolerated by patients

PTX-35

PRECLINICAL DATA

TNFRSF25

An Emerging Target for T-cell Co-stimulation

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)	FDA clearance of PTX-35 IND expected in Q2, 2020 in advanced solid tumors

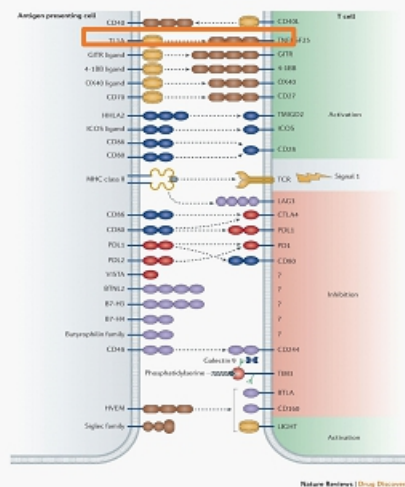
- TNFRSF25 is a potential best-in-class T cell co-stimulator due to its **preferential specificity to 'memory' CD8+ T cells**
- **Pelican is the only company** with a disclosed program targeting TNFRSF25

TNFRSF25 as a Novel I/O Combination Target

- TNFRSF25 is one of the most recently discovered T cell costimulators, and is a rapidly emerging target
- Pelican is the only company developing TNFRSF25 agonist antibodies for I/O

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

Comment from Gordon Freeman et al

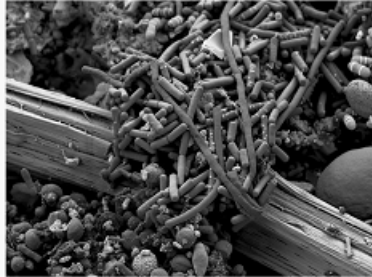


Mahoney K. et al. Nat Rev Drug Discov. 2015

TNFRSF25: Why So Complicated?

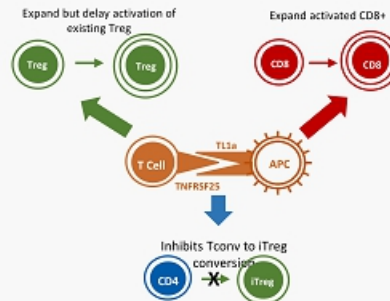
TNFRSF25's evolutionary origin

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



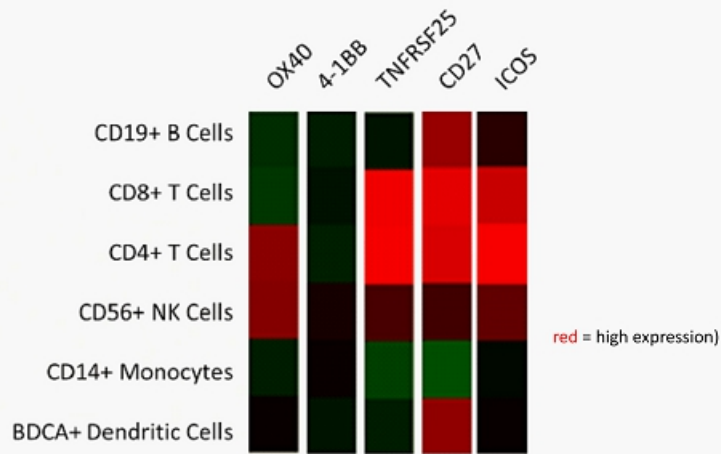
Example: gut invasion occurs in the context of friendly microbiome bacteria. How does the body protect what is needed while weeding out invaders?

One molecule – three types of T-cells



TNFRSF25 is preferentially expressed on CD8+ and CD4+ T-cells

compared to other T-cell co-stimulators



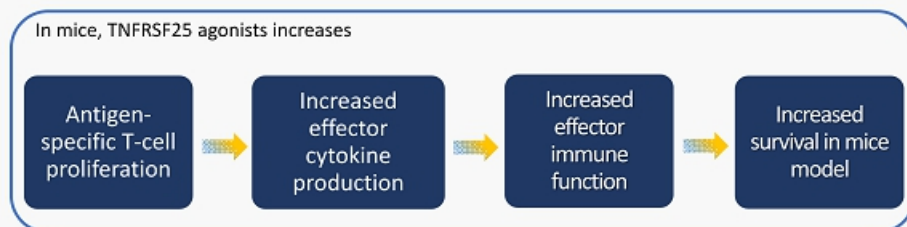
Genomics Institute of the Novartis Research Foundation Su et al. PNAS 2004;101(16):6062-7

PTX-35 Preclinical Data highlights CD8+ T-cell Specificity

TNFRSF25 is preferentially expressed on CD8+ T-cells compared to other T-cell co-stimulators

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

In mice, TNFRSF25 agonists increases

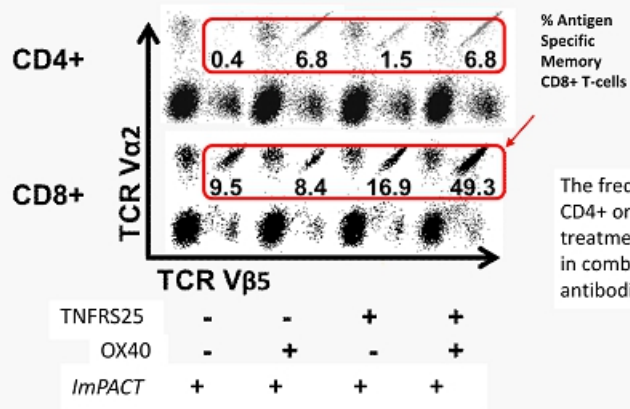


Compared to agonists OX40, GITR, 4-1BB:

- 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

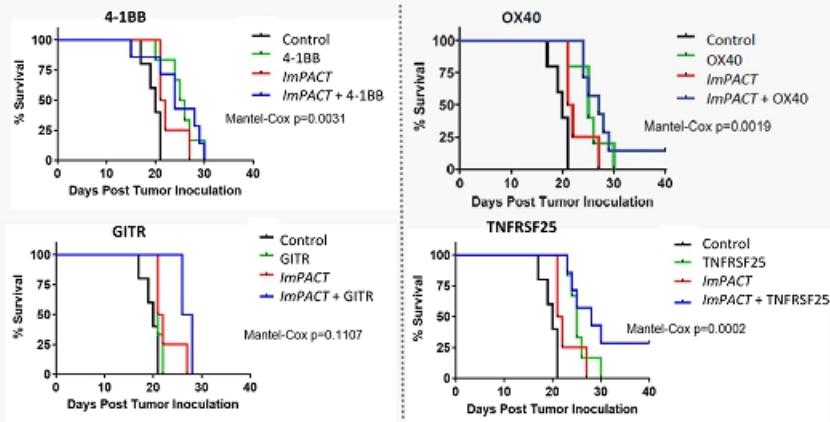


The frequency of antigen-specific memory CD4+ or memory CD8+ T-cells following treatment of mice with *ImPACT*[™] alone, or in combination with OX40 or TNFRSF25 antibodies

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

TNFRSF25 agonist + *ImPACT* Significantly Increases Survival in Mice

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



Schreiber T. et al. SITC 2014

Heat Biologics

NASDAQ: HTBX

CORPORATE PRESENTATION
NOVEMBER 2019

