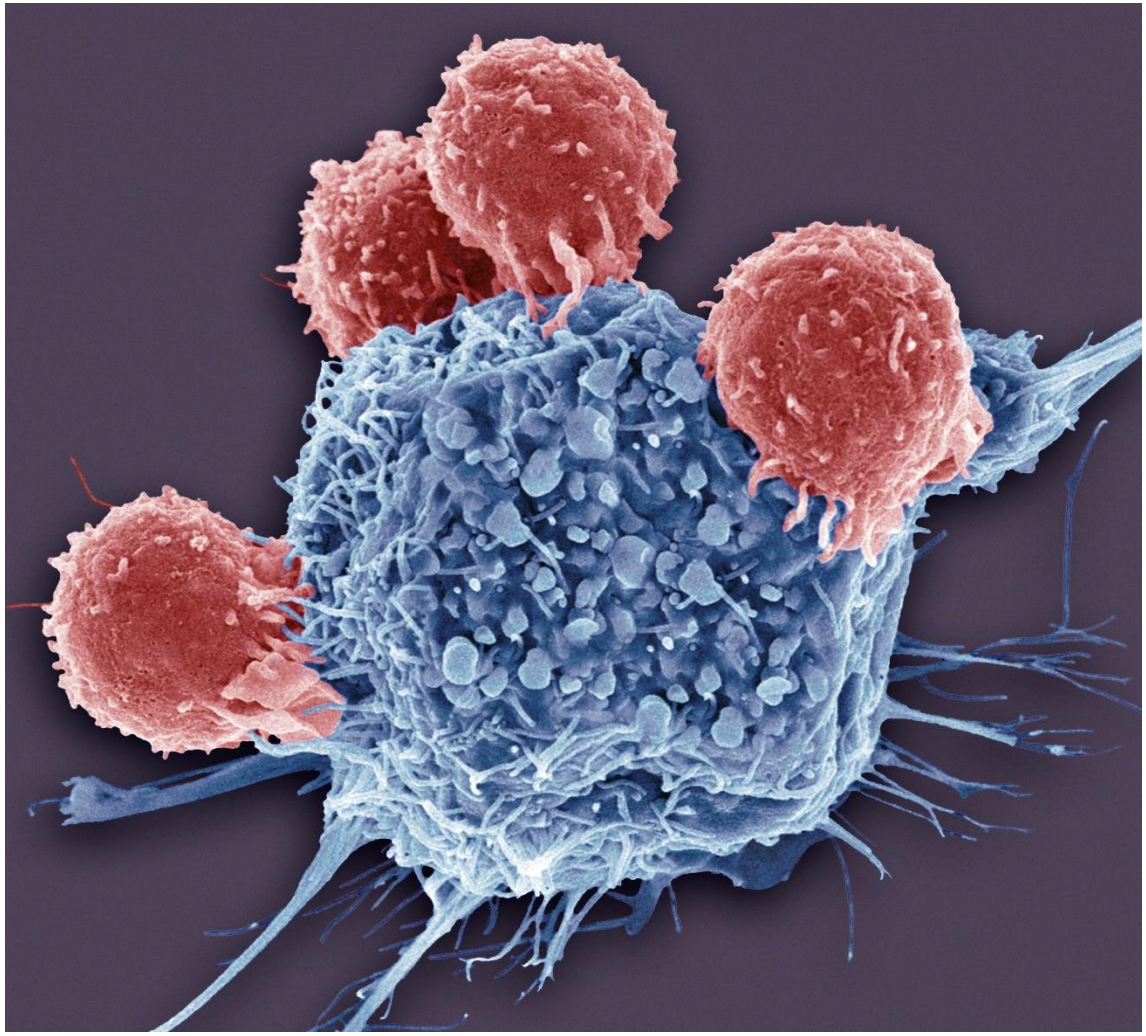
Heat Biologics

Corporate Presentation
February 28, 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.

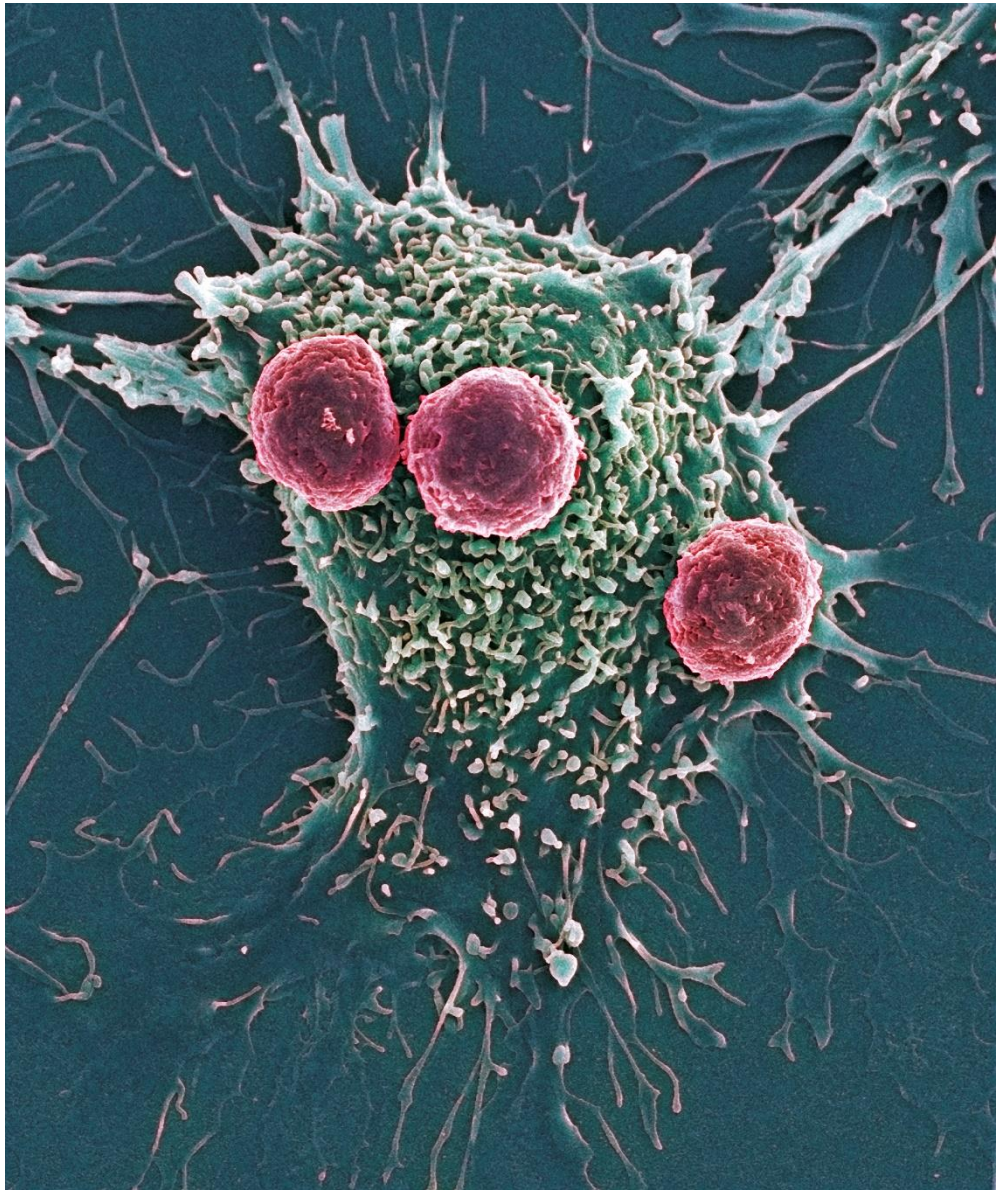
By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines 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 for the year ended December 31, 2017 and our quarterly report on Form 10-Q for the subsequent quarters (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.

You should read carefully the factors described in the “Risk Factors” sections of our SEC Filings to better understand the risks and uncertainties inherent in our business.

Our Mission

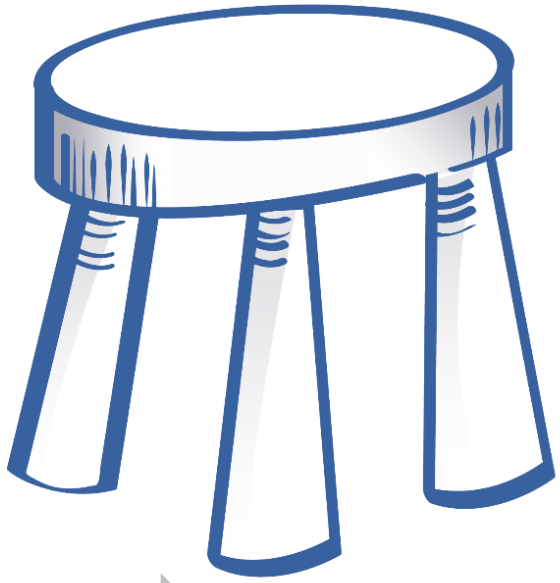
To improve patient outcomes by developing more effective immunotherapies designed to

Turn "COLD" tumors "HOT



Effective Immuno-Oncology Therapy

The three legs of an Immuno-Oncology Stool



T-cell Activation

Heat's Core Focus

Co-stimulation

Checkpoint Inhibition

Combination Therapies

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

T-cell Activation

Co-Stimulation

***ImPACT®* Therapy**

Cell-based Delivery of Multiple Antigens

Activation of Patients' CD8+ "Killer" T-cells

Pelican **PTX-35**

Monoclonal Antibody

Pelican **PTX-45**

Fusion Protein

***ComPACT™* Therapy**

Cell-based Delivery of Multiple Antigens

Activation of Patients' CD8+ "Killer" T-cells

Co-Stimulation to Enhance T-cell Activation and Expansion

Heat Technologies

Combined with

Checkpoint Inhibitors

PD1/PDL1

CTLA-4

Lag-3

TIM-3

Plus others

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)
PTX-45	TBA					TL1A-Ig fusion protein, functional agonist of human TNFRSF25

ImPACT® "Off-the-shelf" Manufacturing

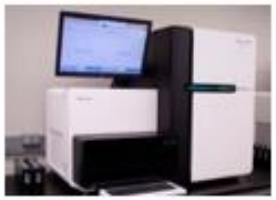
Designed for Robust, Pan-antigen T-cell Activation

Sample

Collect Cancer Cell Line & Patient Tissue Samples

Screen

Compare Using Our Proprietary Technology



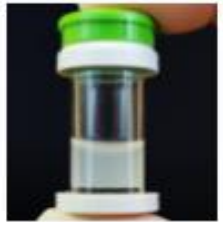
Select

ID Cell Line with Most Antigen Overlap

Transfect with Activation Technology

Scale

Scale-up for Manufacturing by CMO

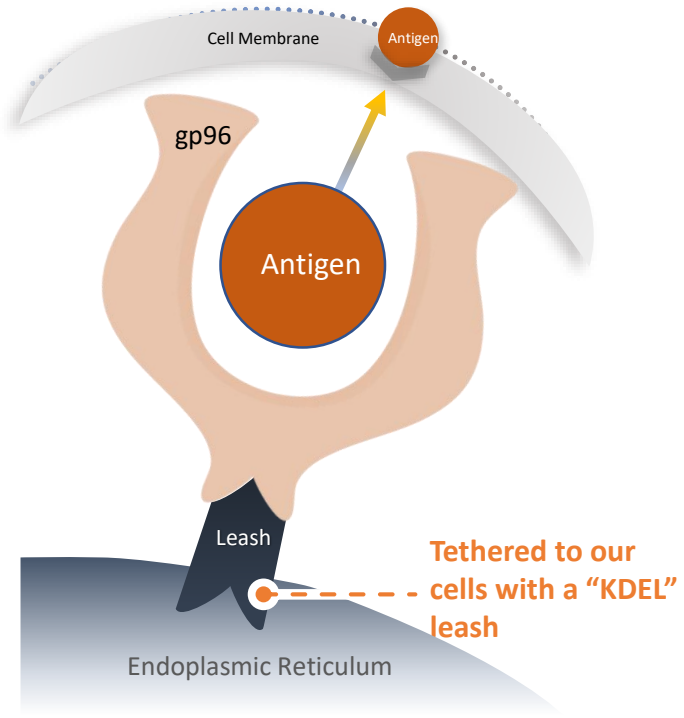


- Frozen, fully-diluted single-dose vial
- Final drug product: 10 million cells
- Easily scaled manufacturing

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

Introducing gp96 – Its dual role

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



"Molecular Warning System"

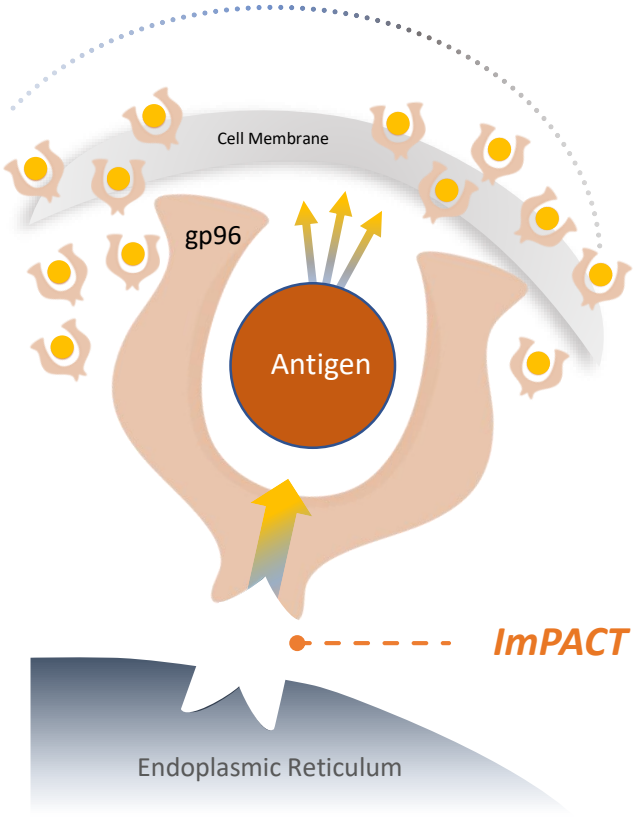
- A natural biological process to deliver proteins (antigens) & gp96 to our immune system
- Gp96 "chaperones" newly-created proteins to the cell membrane where they are released and embedded
- Gp96 chaperoned proteins are only naturally released via necrosis
- Gp96, when present outside the cell, alerts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

ImPACT Platform

"Severing the Leash"

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



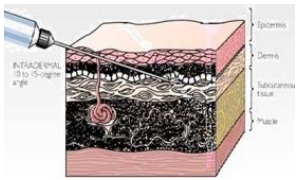
***ImPACT*® technology** genetically modifies tumor cells by "severing the leash" that binds the gp96 to the endoplasmic reticulum, and replacing it with a secretory sequence that pumps gp96 out of the cell

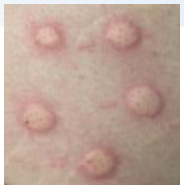
Mimics necrotic cell death by enabling fully-allogeneic "off-the-shelf" living cancer cells to "pump-out" their own antigens along with their gp96 chaperone

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

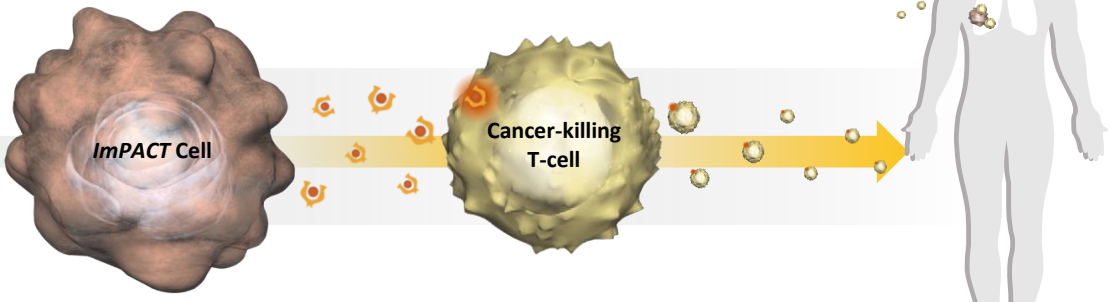
Designed to activate a powerful pan-antigen cytotoxic T-cell immune response

ImPACT®: Immune Pan-antigen Cytotoxic Therapy



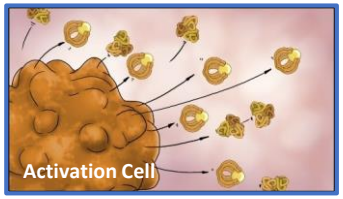


Cluster of five 0.1 mL intradermal injections

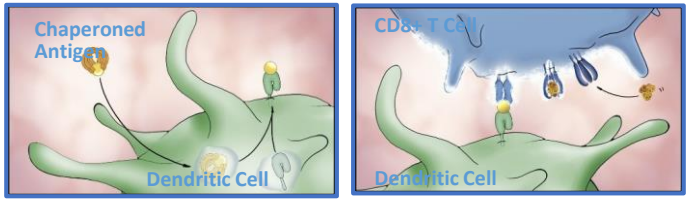


ImPACT cells secrete antigens designed to specifically activate patient's killer T-cells

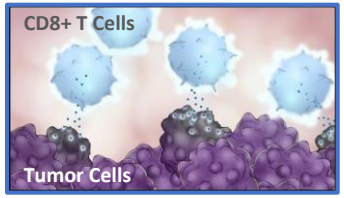
T-cells circulate to destroy patient's tumor



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

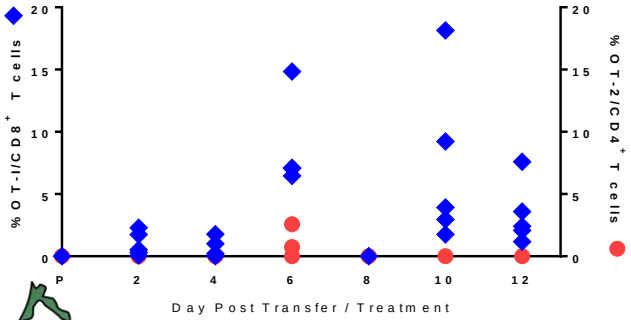
Heat's unique cell-secreted gp96 firstly activates dendritic cells via TLR signaling and subsequently CD8+ T cells via antigen cross presentation

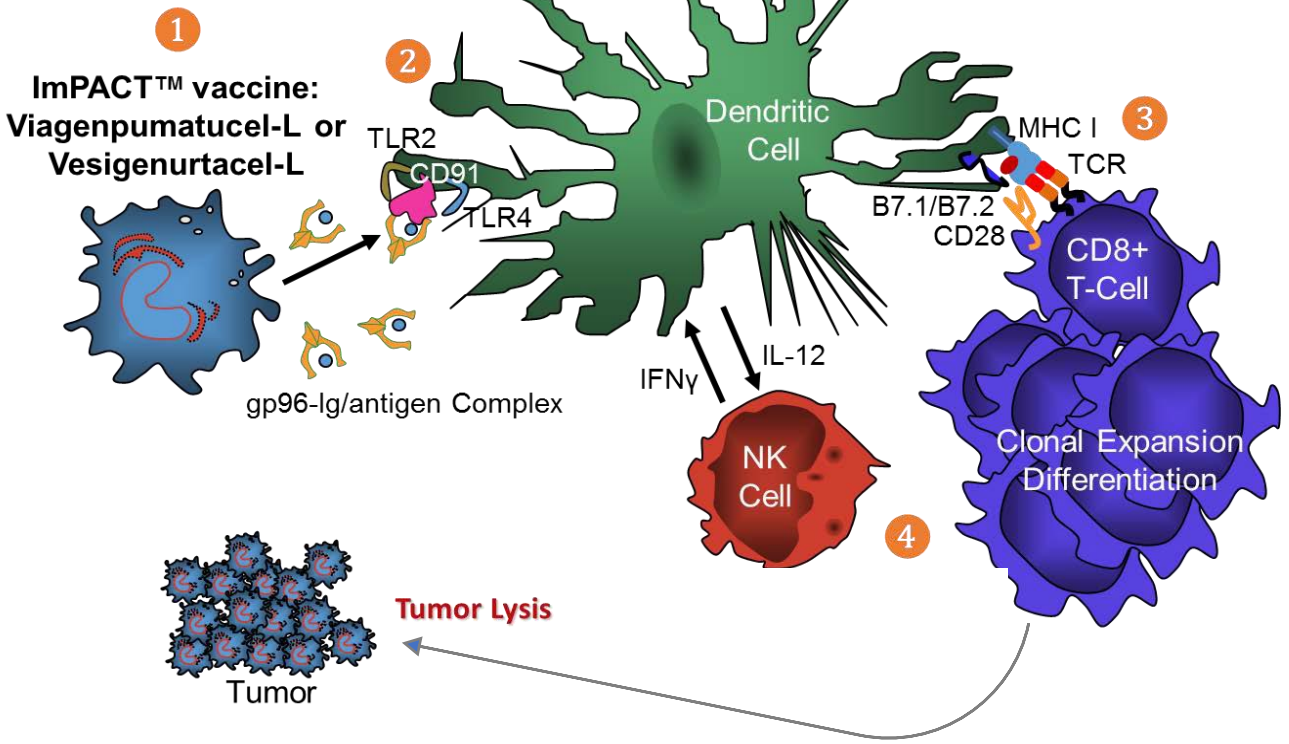
ImPact Generates an Adaptive Immune Response

2 signals Delivered to APCs:

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

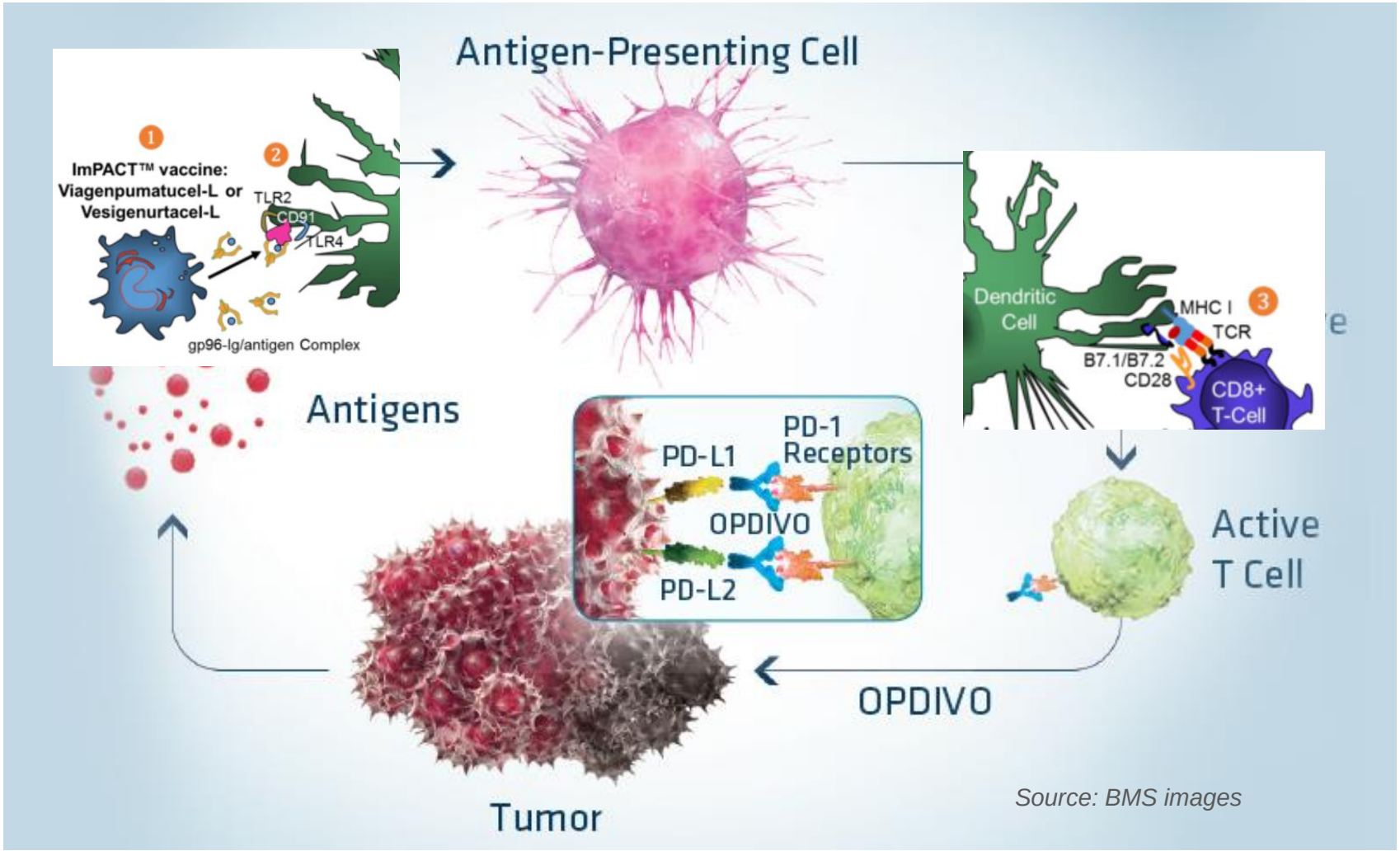
1. **Secretion of gp96-Ig** carrying tumor specific proteins represented on the patients tumor
2. **Activation of APCs** (TLR2/4) and cross-presentation of antigens (CD91)
3. **Specific T-cell receptor** engagement
4. **Clonal Expansion** of Tumor Antigen Specific T cells.





ImPACT + Opdivo Combination Therapy

Potential to improve clinical responses and survival, without additional toxicity



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=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

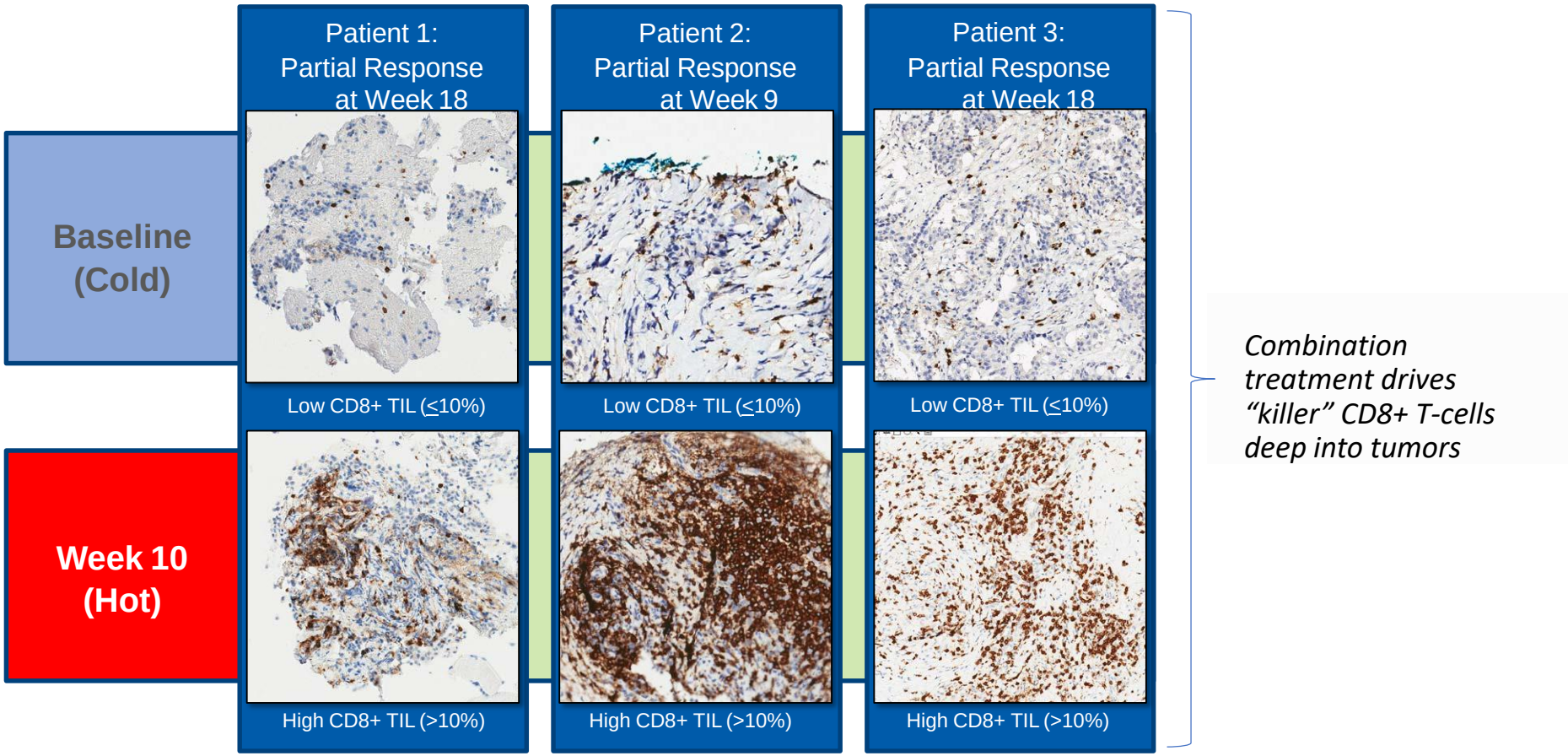
Exploratory Endpoints

Correlation of clinical outcomes to the following factors

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

Clinical Support for HS-110 + Nivolumab Mechanism of Action

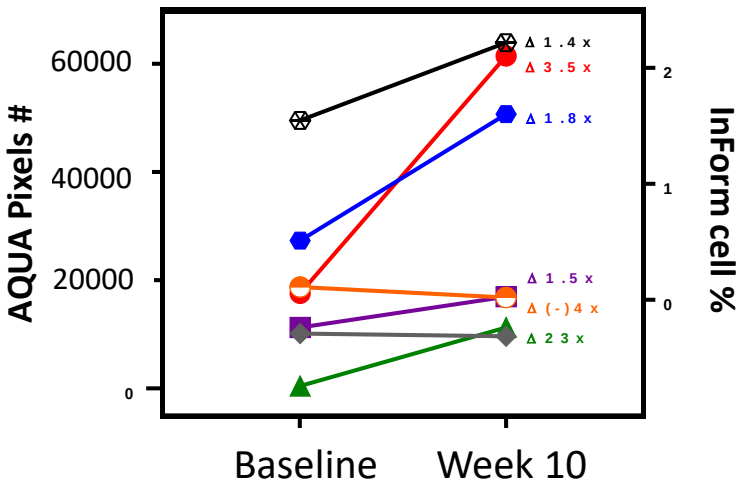
"Turning COLD Tumors HOT"



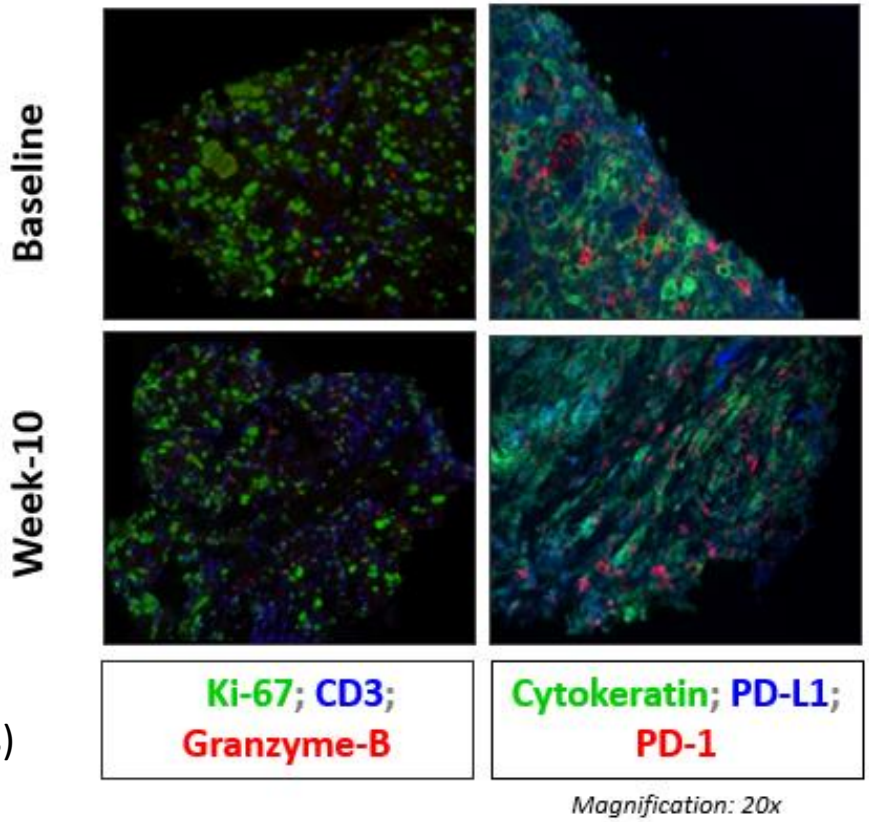
CD8+ TIL Infiltration Associated with Clinical Response

Combination Treatment Substantially Increased Killing Activity in Patient Tumor Microenvironment

RECIST 1.1 Stable Disease for 19+ months



- CD3+ TILs
- CD3+ Ki67 TILs
- PD-1+ Cells
- CD3+ Granzyme B + TILs
- PD-L1+ Tumor Cells
- CD4+ Foxp3+ Cells (Tregs)
- CD4+ T cells



Magnification: 20x

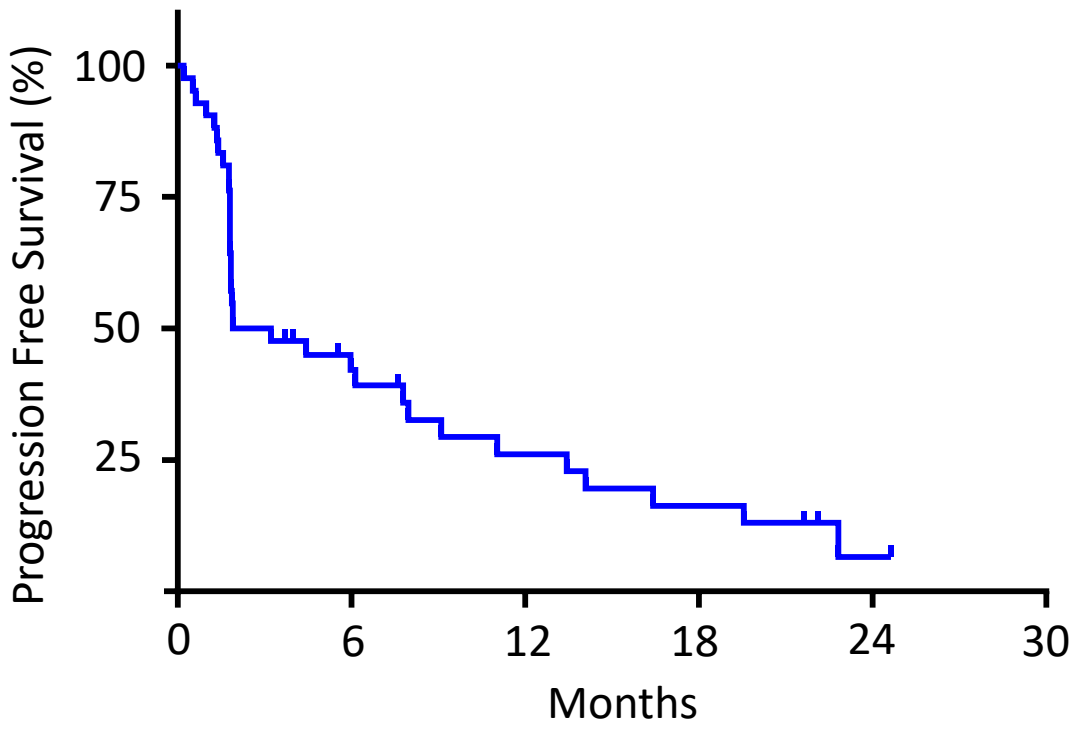
Substantial increase of CD3+ TILs and CD3+ Granzyme B+ TILs for enhanced tumor killing activity

Pathology analysis performed by Yale School of Medicine

Cohort A:

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

Progression-Free Survival (PFS)



N=42 (All patients enrolled)

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

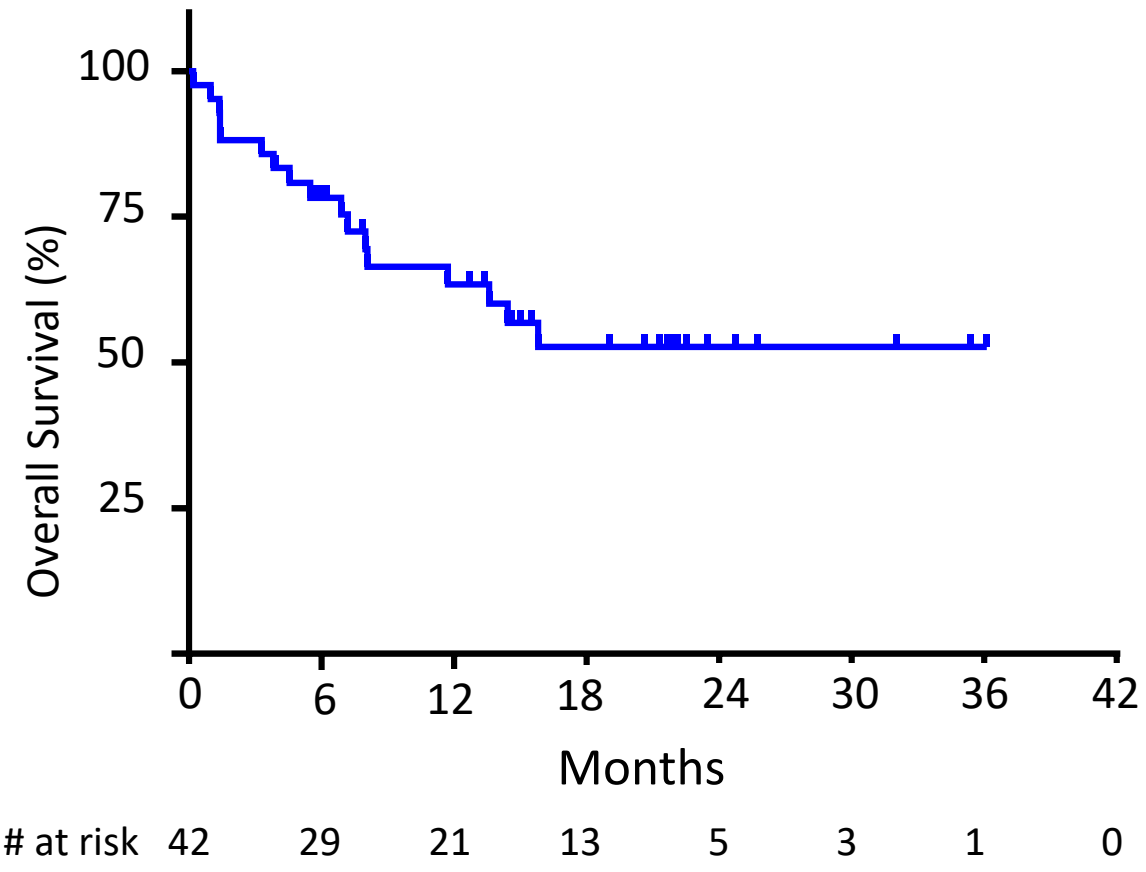
Median PFS of nivolumab alone
2.3 months *
(95% CI: 2.2 – 3.3 months)

* 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)



N=42 (All patients enrolled)

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

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

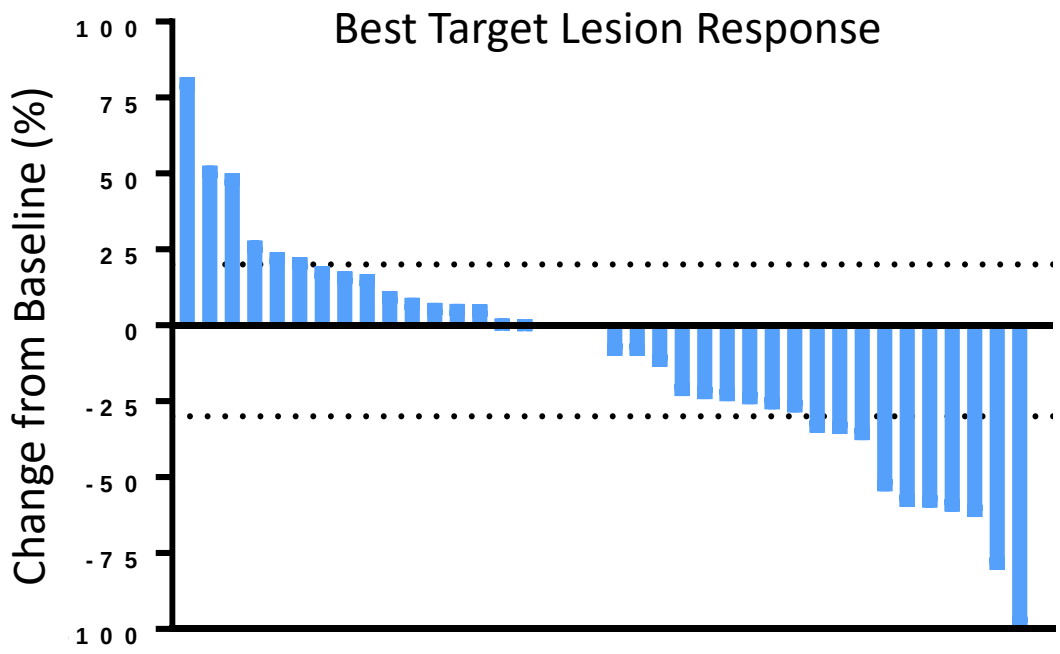
Median OS of nivolumab alone 12.2 months*
(95% CI: 9.7 – 15.0 months)

*Borghaei et al. 2015 *NEJM*

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)

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

PR	9 (21%)
SD	12 (29%)
Not evaluable	4 (10%)
DCR	**21 (50%)**

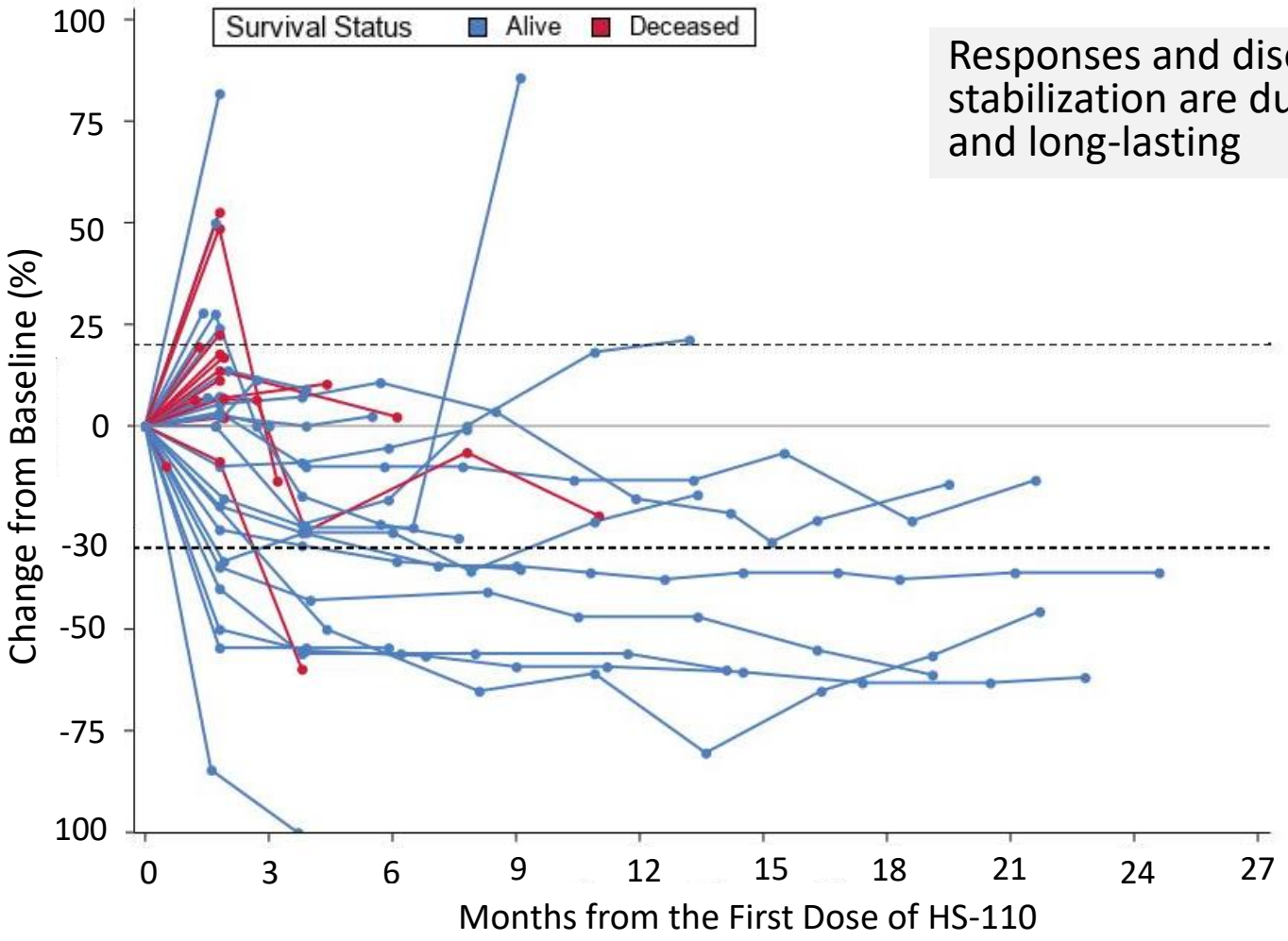
Nivolumab alone in CPI naïve patients*
ORR = 19% (95% CI: 15% - 24%)
DCR = 44%

**Borghaei et al 2015 NEJM*

Cohort A:

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

Duration of Benefit



Responses and disease stabilization are durable and long-lasting

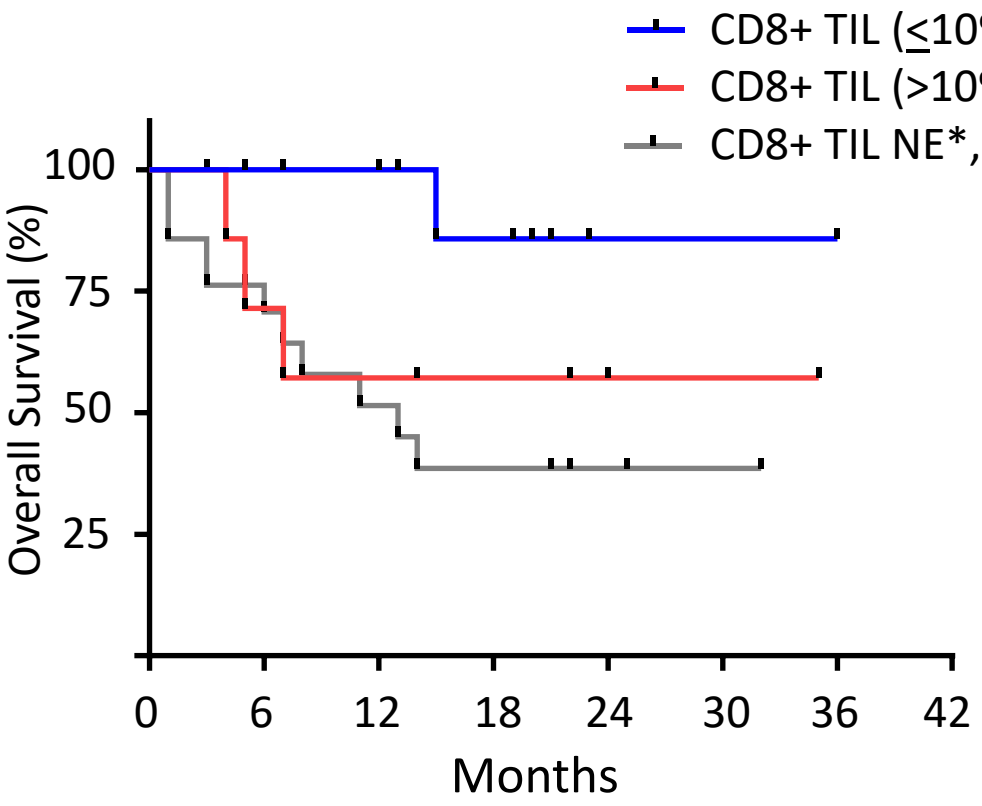
Heat Biologics

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



	Low CD8+ TIL (≤ 10%)	High CD8+ TIL (> 10%)
Median OS	NR	NR

HR 0.39
(95% CI: 0.06 – 2.31)

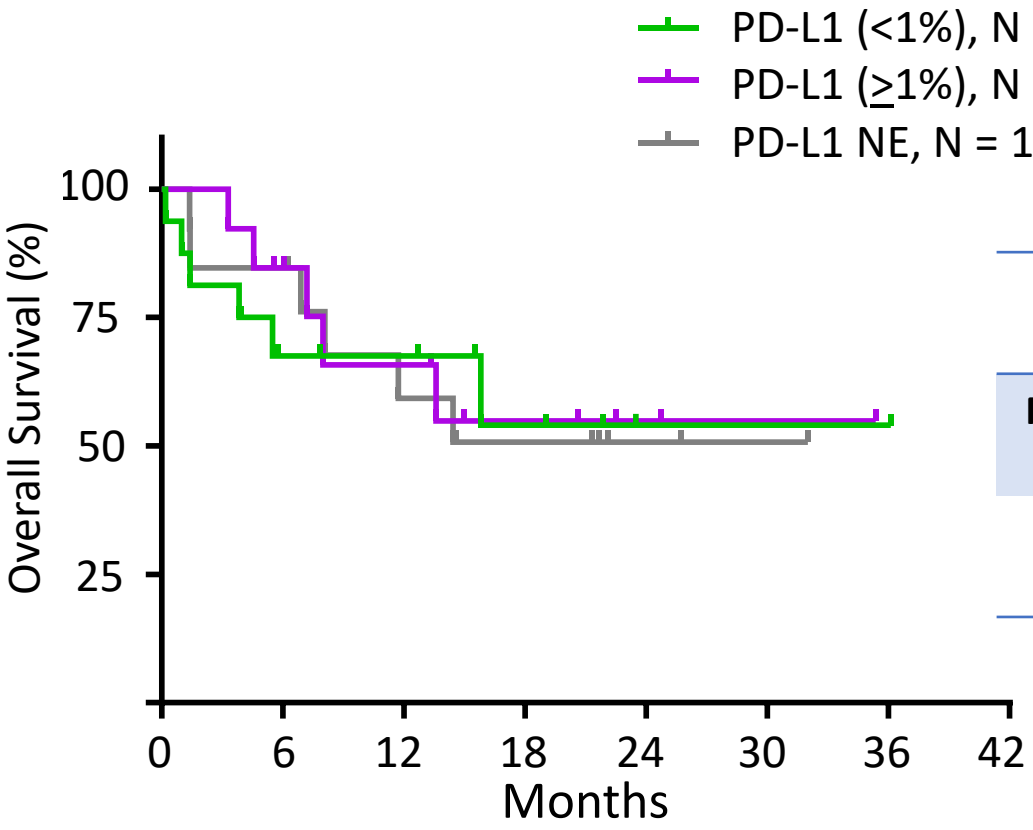
*TIL NE = Tumor infiltrating lymphocyte not evaluable

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

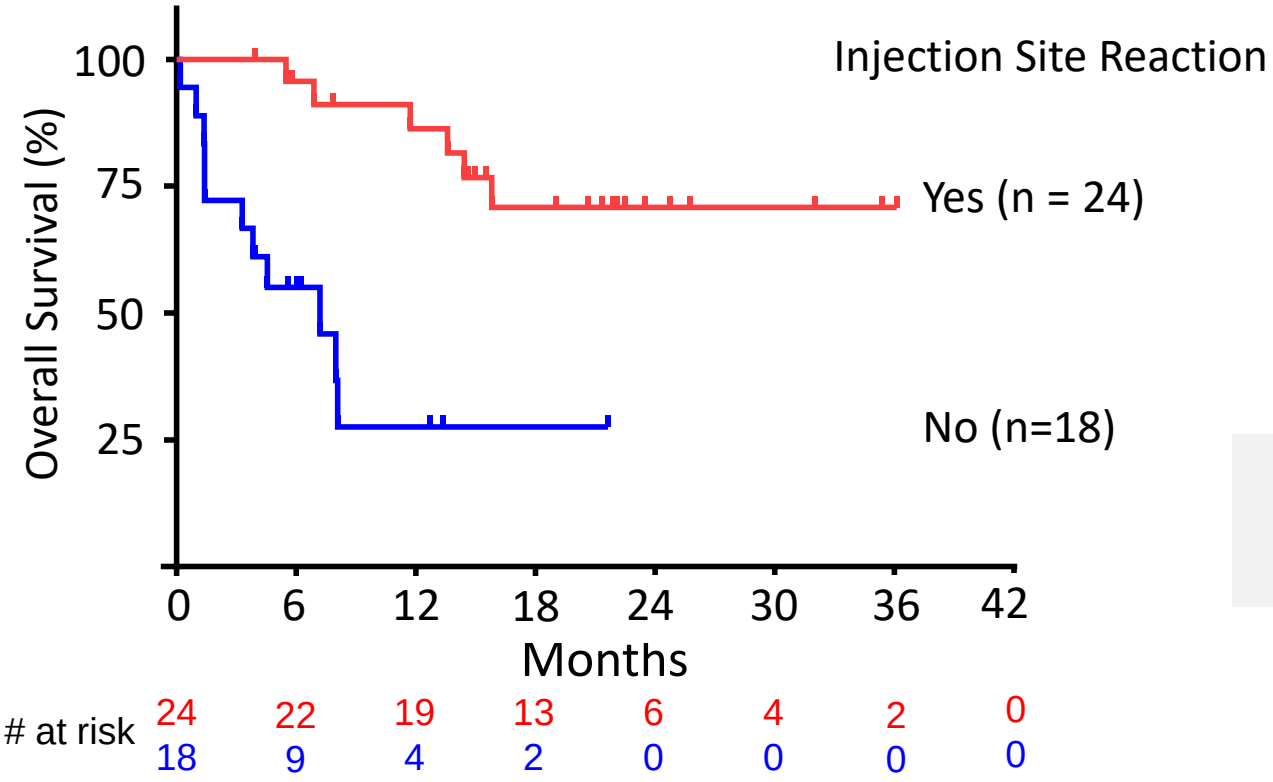


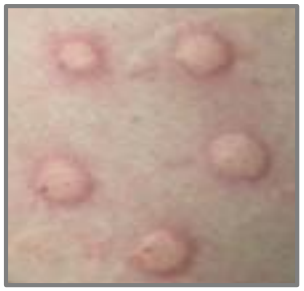
	Negative PD-L1 (< 1%)	Positive PD-L1 (≥ 1%)
Median OS	NR	NR
	HR 0.85 (95% CI: 0.26 – 2.79)	

Cohort A:

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

OS by Injection Site Reaction (ISR)





Typical Injection Site Reaction

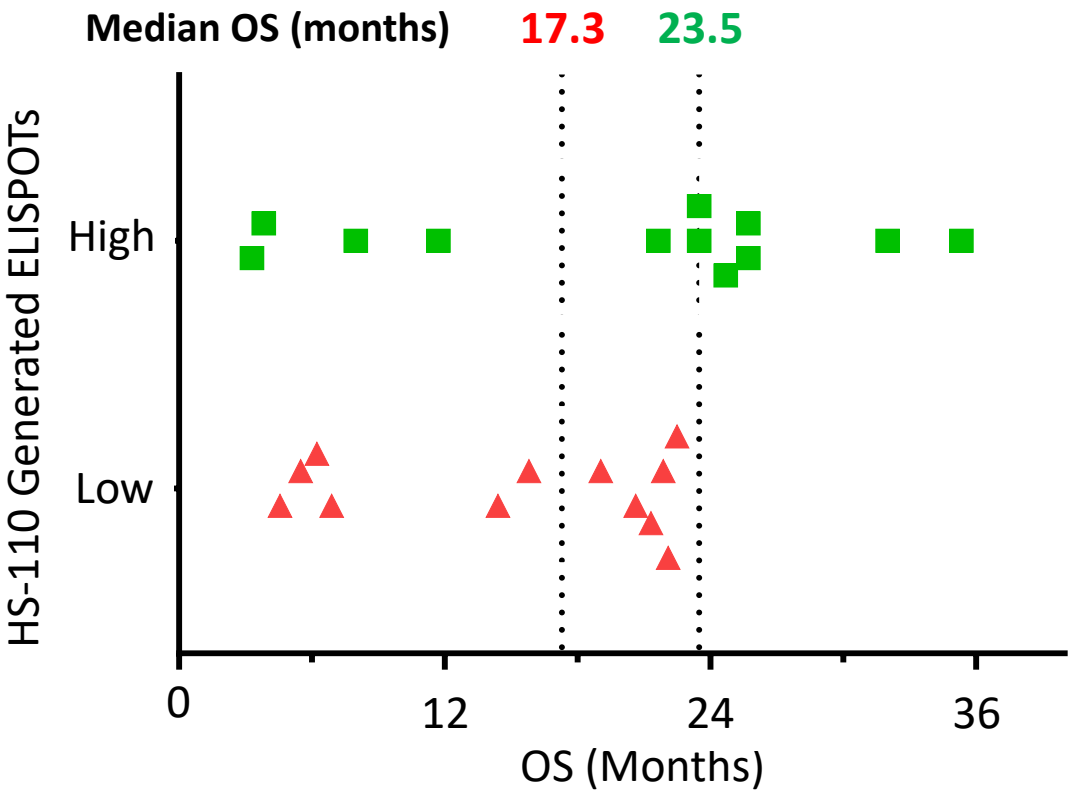
mOS: NR vs. 7.2 months
HR: 0.15 (95% CI: 0.05-0.45)
p = 0.0001

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

Cohort A:

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

Survival Benefit with Increased Immune Activity



Peripheral blood obtained before and during treatment to measure HS-110 derived immune reactivity.

ELISPOTs represent INF-ɣ secretion from T cells in culture after stimulation with HS-110 lysate.

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

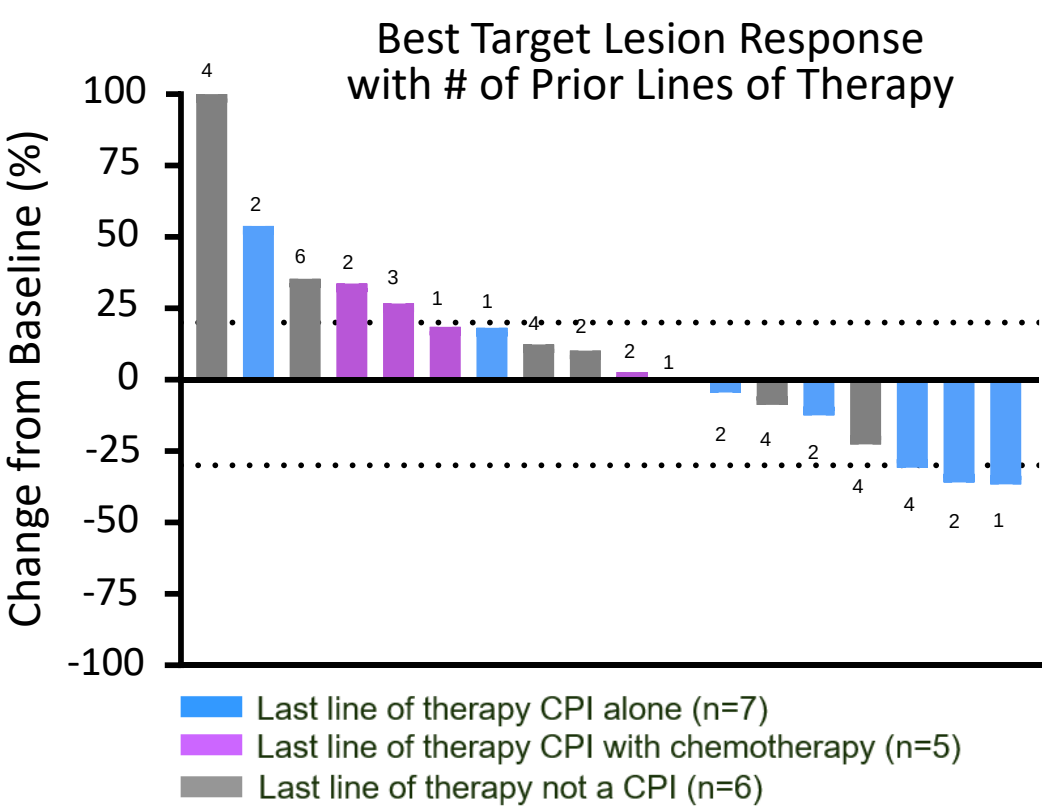
Low = Patients with absolute ELISPOT increases **below** the group median

A 6-month improvement of median survival in patients with high HS-110 stimulated immune activity

Cohort B:

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

Objective Response Rate



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

PR*	4 (20%)
SD	7 (35%)
Not evaluable	2 (10%)
DCR	**11 (55%)**

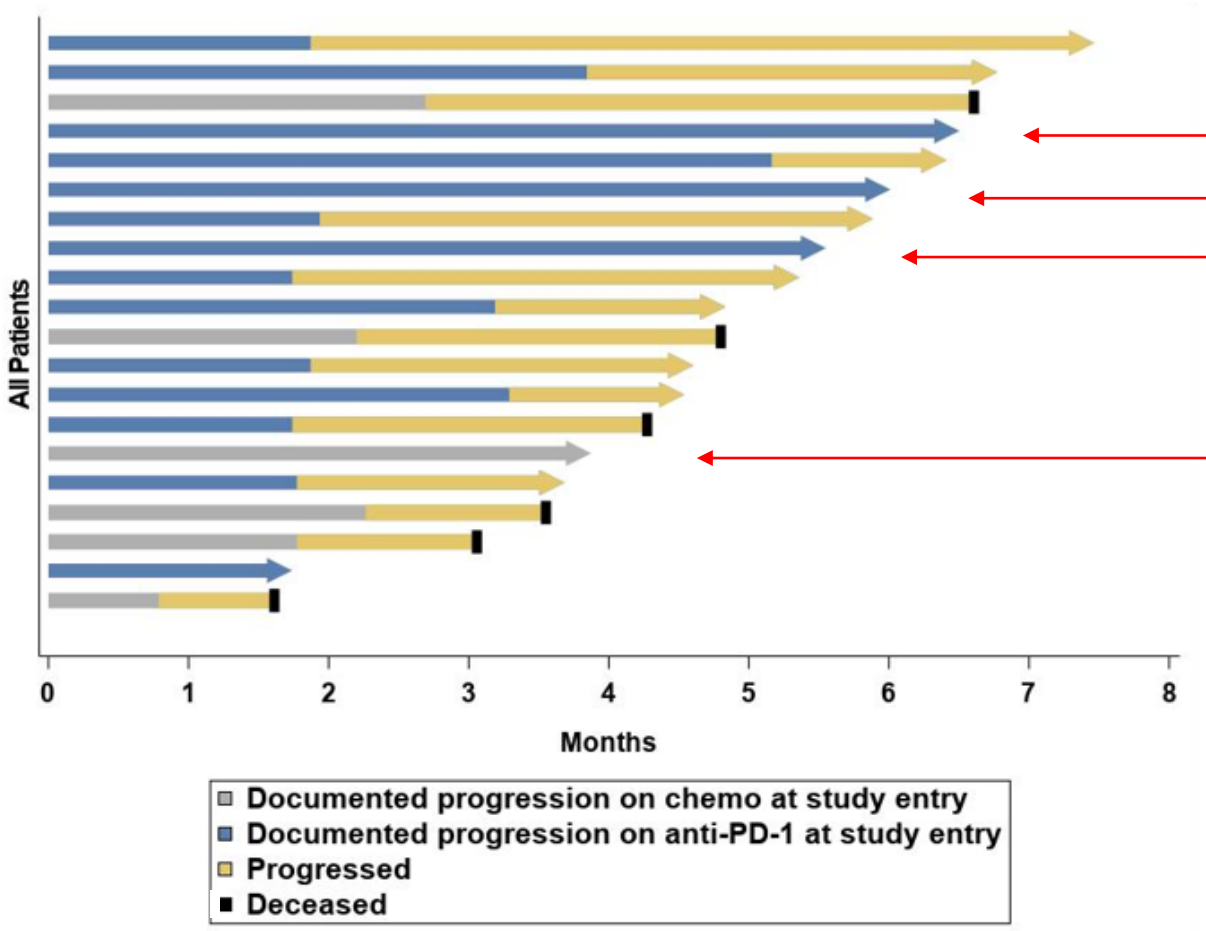
* Per Investigator assessment

- Stabilization of disease in > 50% of patients
- Response rates suggest that addition of HS-110 can restore responsiveness to CPI therapy
- The 3 RECIST partial responses were in patients who failed CPI immediately preceding study entry

Cohort B:

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

Duration of Clinical Benefit



4 out of 20 patients have not progressed on therapy

Median Progression-Free Survival (PFS)
2.7 months
(95% CI: 1.8 - 4.0 months)

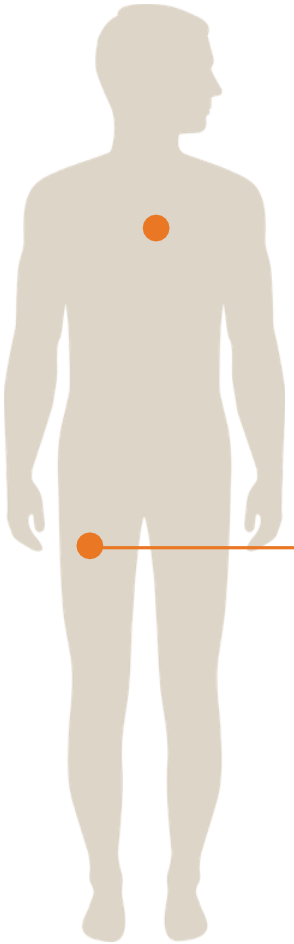
Safety Profile to Date

1,000+ Doses - No Serious Adverse Reactions

Favorable Safety Profile To Date

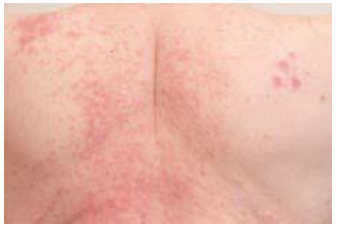
- Over 1,000 doses administered to ~200 patients
- Only one patient ended treatment due to a non-serious adverse reaction*
- No systemic use of steroids required to treat reactions
- No treatment-related serious adverse reactions

No additive toxicities to standard of care



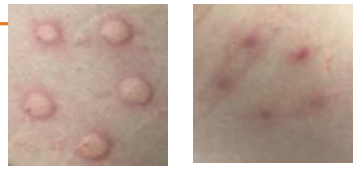
Immune Reaction*

≤ 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 is well tolerated
- Preliminary results demonstrate the ability of HS-110 plus nivolumab to induce CD8+ T-cell tumor infiltration in previously “cold” tumors
- In Cohort A, the occurrence of injection site reactions and increased INF-γ ELISPOTs appears to be associated with improved overall survival
- Data in Cohort B suggests that the addition of HS-110 to nivolumab may restore responsiveness after tumor progression on prior checkpoint inhibitors

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

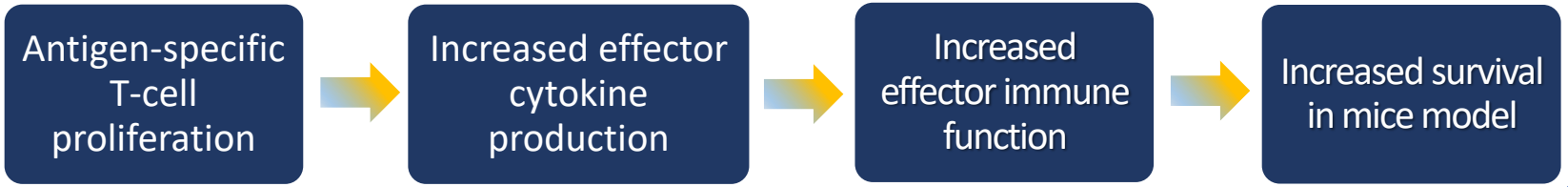
Pre-clinical data of PTX-35 highlights CD8+ T-cell specificity

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)

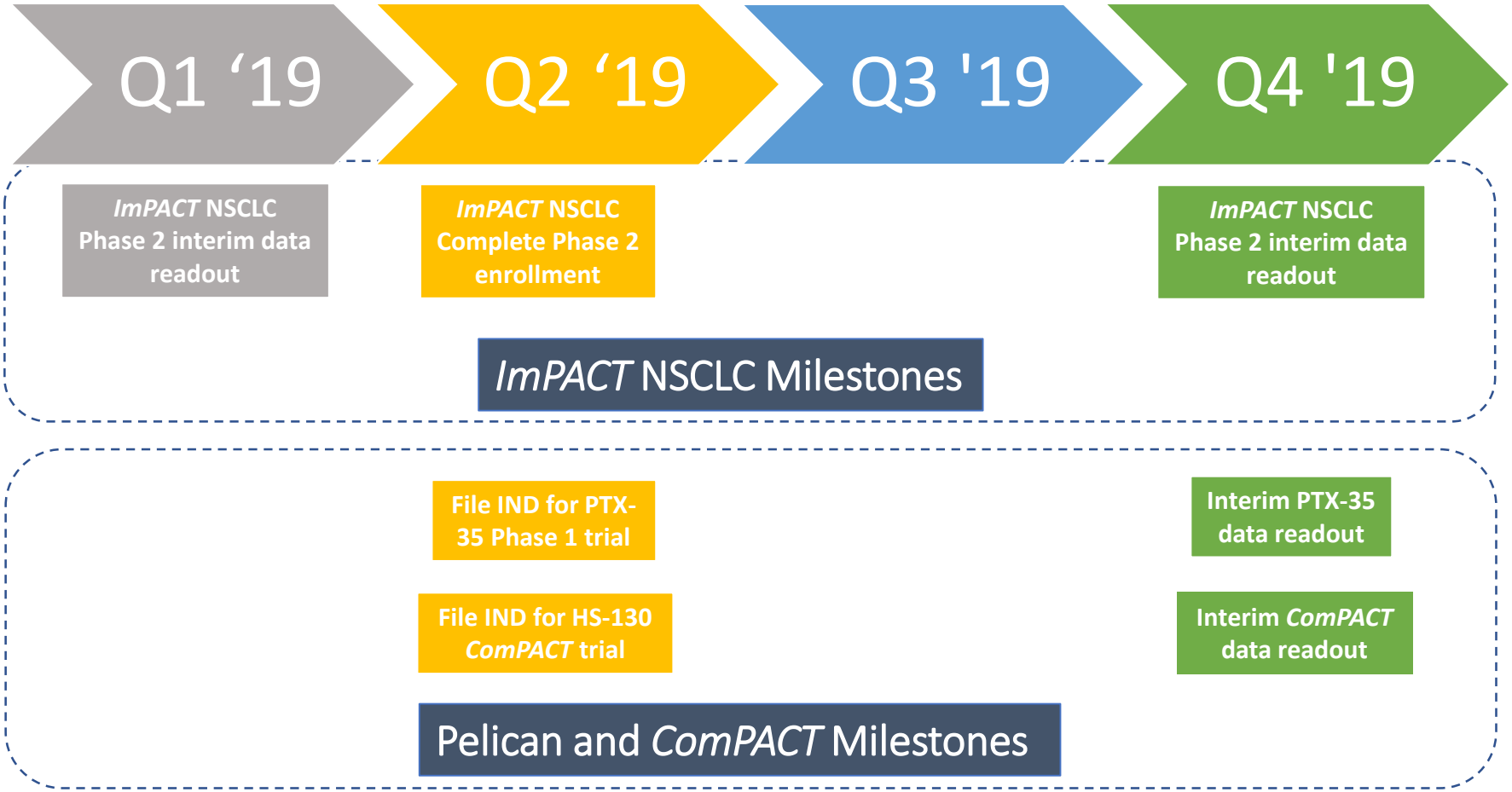
In mice, TNFRSF25 agonists increases



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

Corporate Milestones



Corporate Highlights

Nasdaq	Shares Outstanding	Cash & Equiv.	Founded in	Employees	Grant Awarded
HTBX	**32.5M**	**$27.7M**	**2008**	**30**	**$15.2 M**

Capitalization Table (as of 12/31/2018)	**Shares**
Common shares outstanding	32.5 M
Warrants	9.0 M
Outstanding stock options	3.1 M
Unvested restricted stock	1.6 M
Fully Diluted Shares Outstanding	46.2 M

Investment 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

Cohort A & B: Patient Characteristics

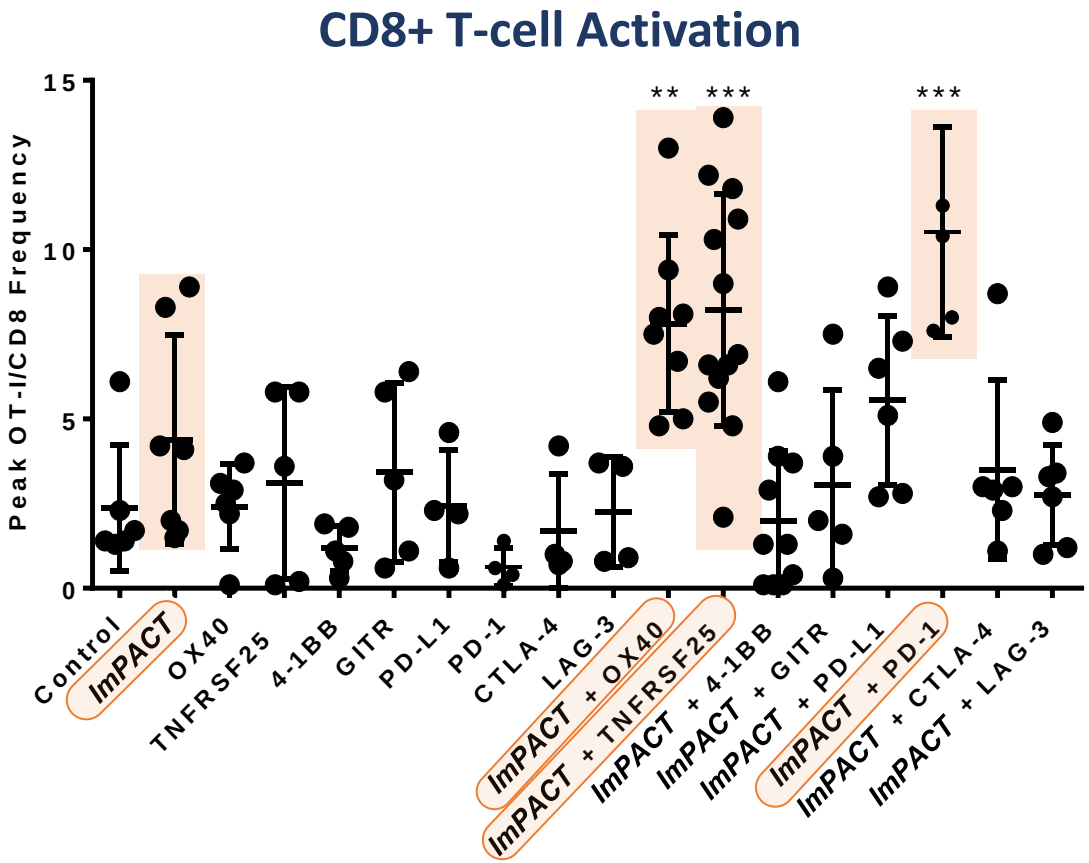
Stage III or IV advanced NSCLC

		Cohort A (N = 42)	Cohort B (N = 20)
Median age (range)		64 (37-87)	65 (56-84)
Female gender		22 (52%)	14 (70%)
Caucasian		38 (90%)	15 (75%)
ECOG PS 1		26 (62%)	10 (50%)
Histology	Adeno	39 (93%)	17 (85%)
	Squamous	3 (7%)	3 (15%)
Smoking Status	Current/past	37 (88%)	17 (85%)
	Never	5 (12%)	3 (15%)

		Cohort A (N = 42)	Cohort B (N = 20)
EGFR or ALK positive		9 (22%)	2 (10%)
Prior lines	1	27 (64%)	3 (15%)
	2 or more	13 (30%)	16 (80%)
	Unavailable	2 (5%)	1 (5%)
PD-L1	< 1%	16 (38%)	7 (35%)
	≥ 1%	13 (31%)	8 (40%)
	Unevaluable	13 (31%)	5 (25%)
CD8+ TIL	≤ 10%	12 (29%)	7 (35%)
	> 10%	8 (19%)	6 (30%)
	Unevaluable	22 (52%)	7 (35%)

Preclinical Data of CD8+ T cell Activation

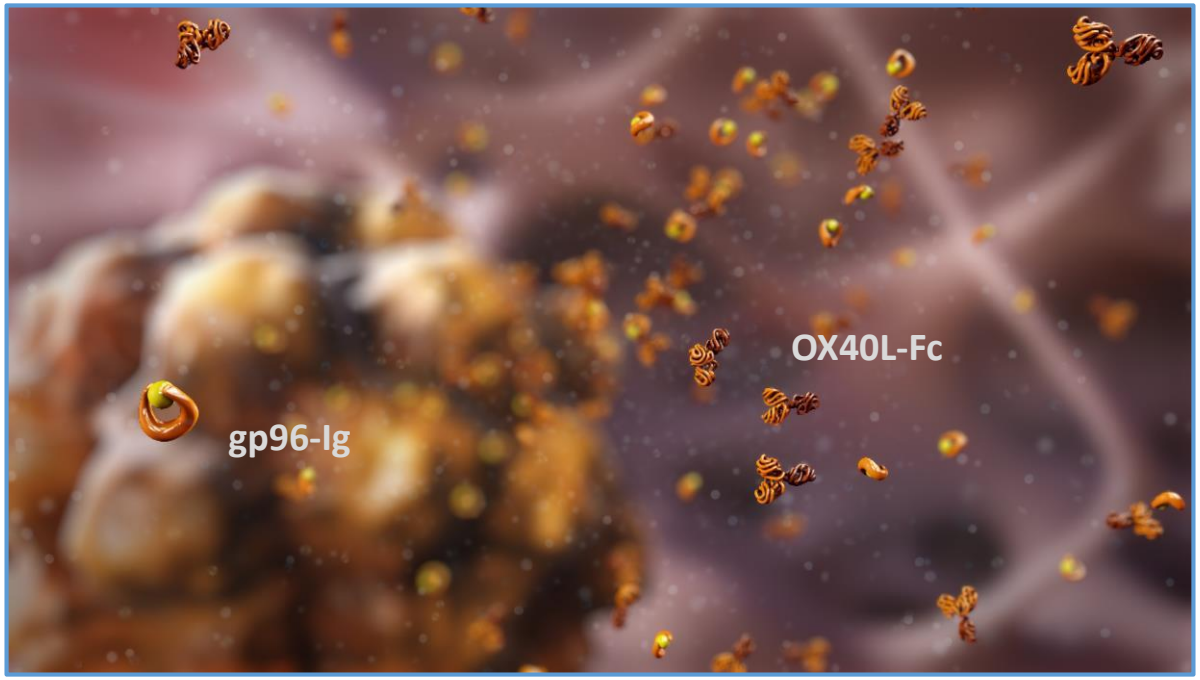
ImPACT® alone and in combination with co-stimulator agonists: OX40, TNFRSF25, PD-1



- 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

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

ComPACT™ Platform Technology

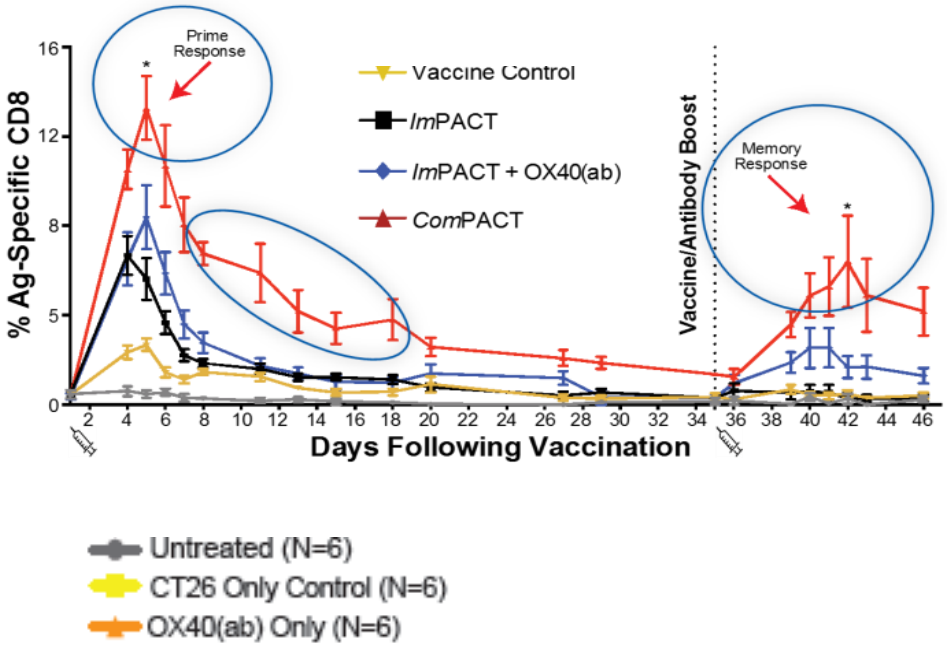


The first potential dual-acting immunotherapy designed to deliver T-cell activation and co-stimulation in a single product – combination therapy without additive costs

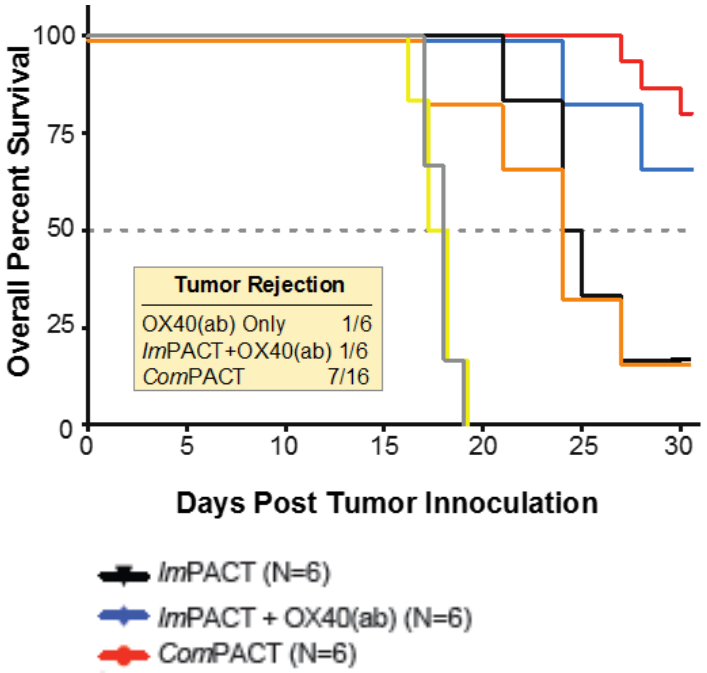
ComPACT™ Outperforms OX40

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**

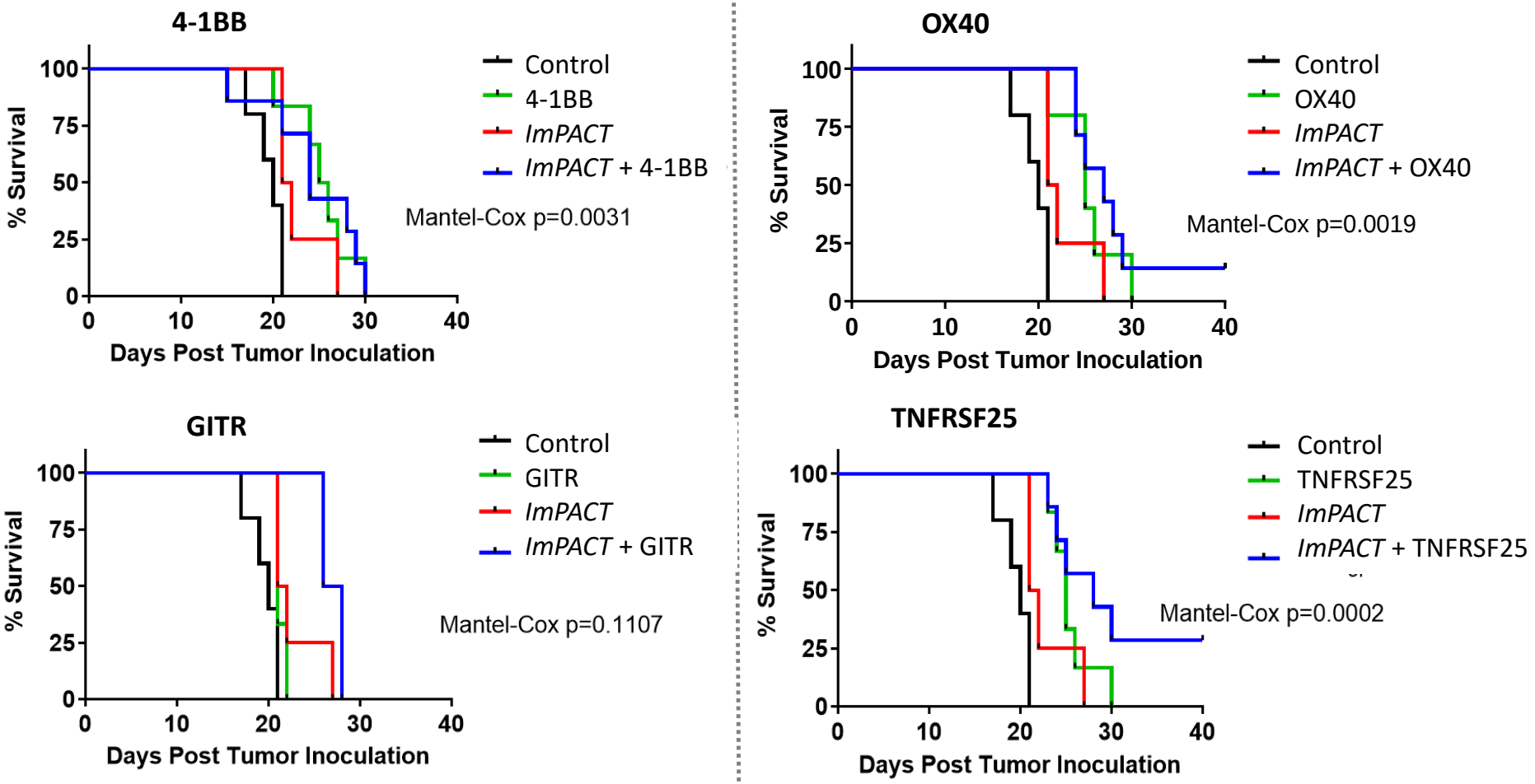
TNFRSF25 - An Emerging Target for T-cell Co-stimulation

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

TNFRSF25 agonist + *ImPACT* Significantly Increases Survival in Mice

Nine-day B16-F10 melanoma model

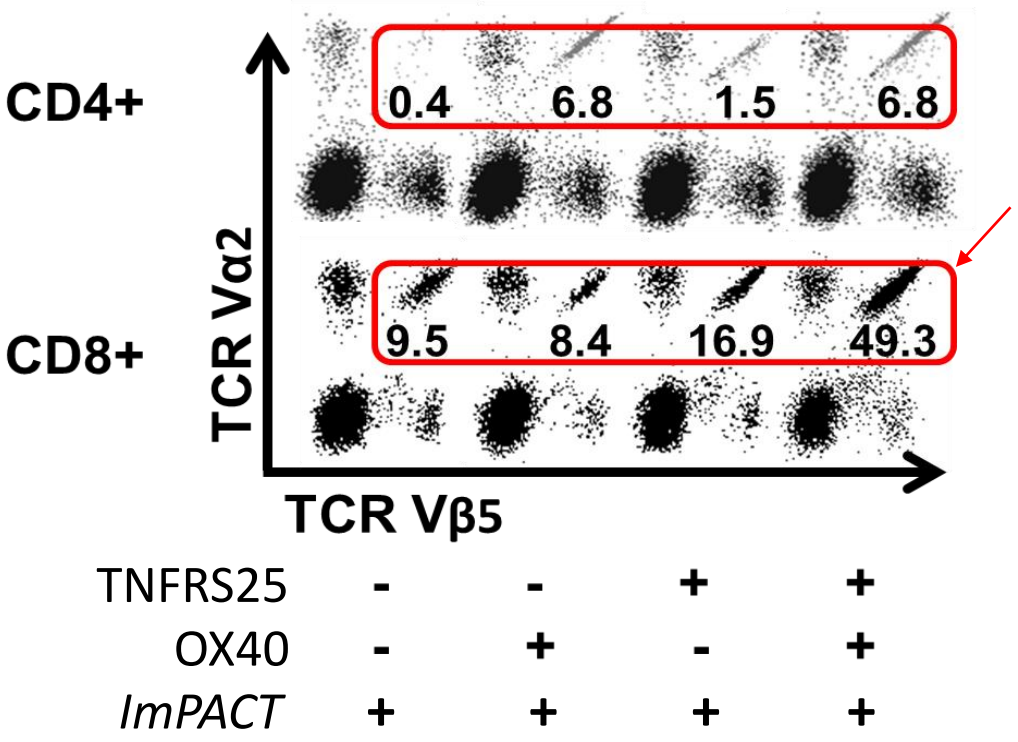


Schreiber T. et al. SITC 2014

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

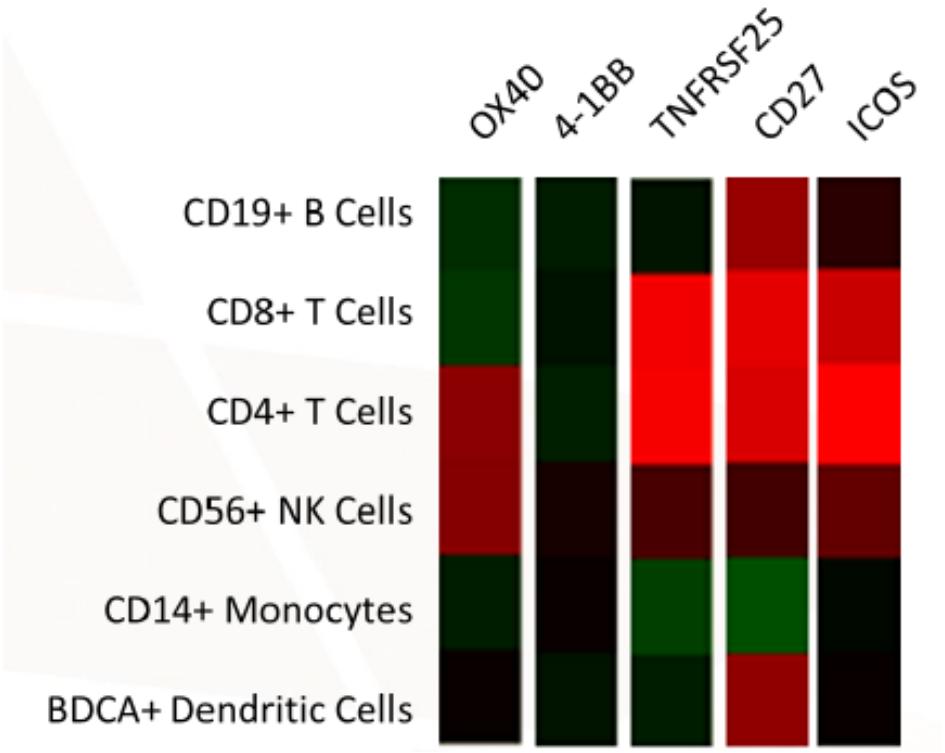


The frequency of antigen-specific memory CD4+ or memory CD8+ T-cells following treatment of mice with *ImPACT™* alone, or in combination with OX40 or TNFRSF25 antibodies

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

TNFRSF25 is preferentially expressed on CD8+ 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

Management and Advisors

Management


Jeff Wolf
Founder & CEO


Jeff Hutchins, Ph.D.
CSO/COO


George Peoples, MD
Chief Medical Advisor


Ann Rosar
VP of Finance


Janice McCourt
VP of Business Devt.


Lori McDermott
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