Heat Biologics

NASDAQ: HTBX

CORPORATE PRESENTATION

FEBRUARY 2021

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, autoimmune diseases and infectious diseases, our planned discovery and development of a COVID-19 vaccine, 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, 2019, 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)

- **US-based biopharmaceutical company developing 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 therapy**
  - Ongoing Phase 2 program demonstrates positive survival data in PD-(L)1 naïve and PD-(L)1 progressor patients
- **HS-130 is the first allogeneic, off-the-shelf, cell therapy approach utilizing OX40-mediated co-stimulation to enhance activation of dormant immune signals**
  - Phase 1 in solid tumors currently enrolling
- **COVID-19 vaccine program aims to engineer multiple viral protein regions into our gp96 platform**
  - Target to generate long-term innate and adaptive immune responses; currently in preclinical development
- **PTX-35 for T-cell activation and co-stimulation**
  - Phase 1 trial in solid tumors currently enrolling
  - Preclinical synergy with anti-PD-(L)1 when combined with antigen-driven 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 + CTAs (Cell Therapy)	NSCLC				
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CTA = cancer testis antigen; NSCLC = Non-small cell lung cancer

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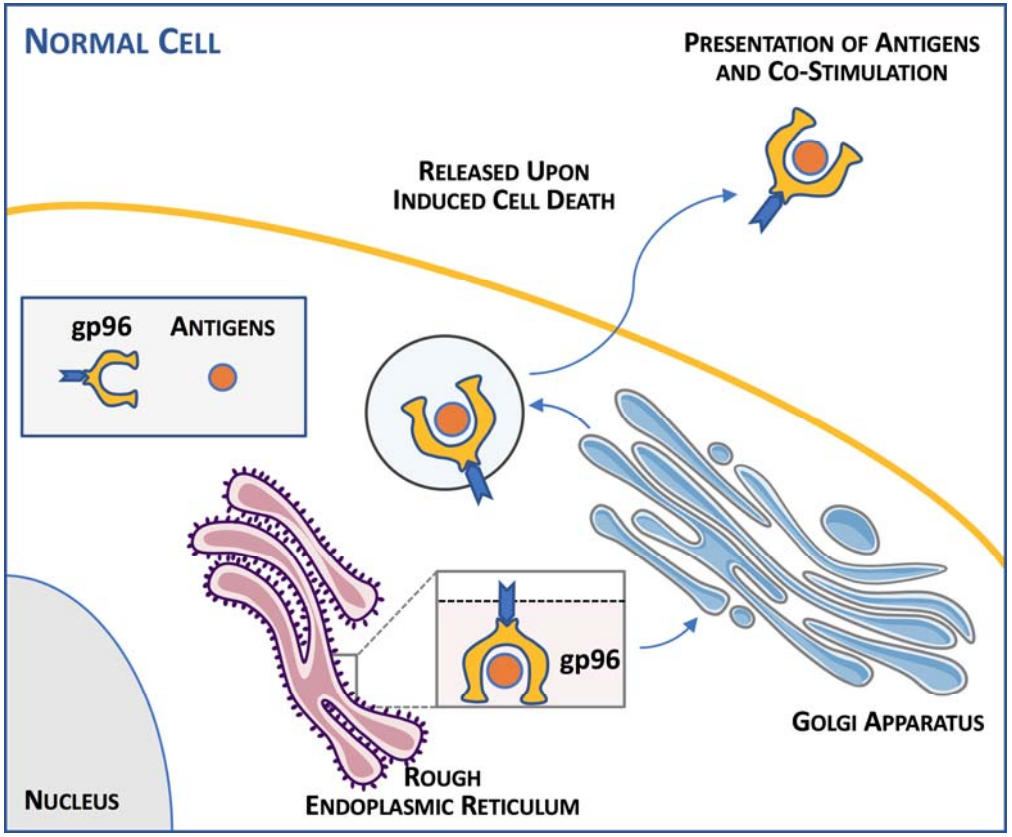
HS-110 Overview

- **HS-110 is a Phase 2 cell-based immunotherapy administered in combination with PD-(L)1 therapy to improve clinical outcomes for NSCLC patients**
  - Allogeneic cells with engineered gp96 to present multiple 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**
- **Combination of HS-110 and PD-(L)1 therapy may benefit patients in multiple treatment settings**

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; ǂ Shukuya & Carbone 2016. Journal of Thoracic Oncology, Vol.11 No.7: 976 - 988

Heat Biologics' gp96 Platform

Activating the Immune System



- Function of heat shock protein gp96:
  - Potent mucosal adaptive memory inducer
  - Chaperones antigens (pathogens or tumor) to the immune system
  - Activates B cell response and drives antigen-specific CD4+ and CD8+ T cell activation

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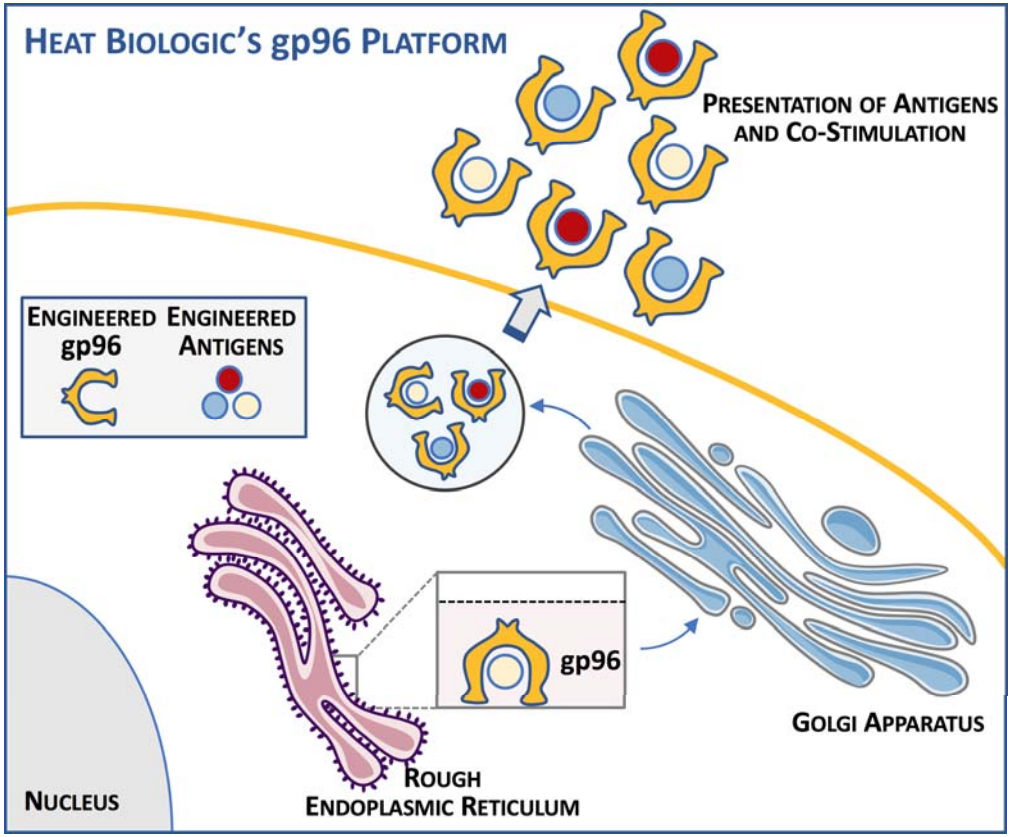

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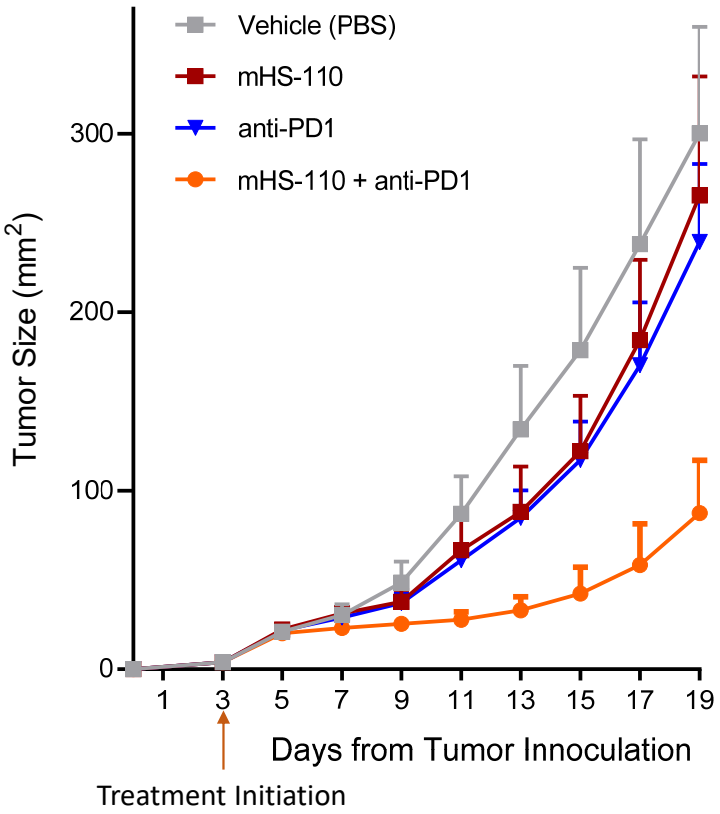
  - Chaperones antigens (pathogens or tumor) to the immune system
  - Activates B cell response and drives antigen-specific CD4+ and CD8+ T cell activation
- Key features of Heat's gp96 platform
  - Leverages gp96's role as a natural molecular warning system
    - Engineered to secrete antigens bound to gp96
  - Off-the-shelf allogeneic cell vaccine
    - Feasible for large scale manufacturing
    - Amenable to stockpiling
  - Broad applications in infectious diseases and cancer
- Lead product in Phase 2 trial for NSCLC

Synergy of HS-110 with PD-1 Inhibitor

B16F10 Syngeneic Mouse Melanoma Model



- B16F10 mouse model is a very aggressive tumor model and is resistant to anti-PD1 treatment
- Synergistic anti-tumor-growth activity of mouse HS-110 with anti-PD1 was demonstrated as compared to either agent individually
- Anti-PD1 or HS-110 as a single agent did not significantly inhibit tumor growth

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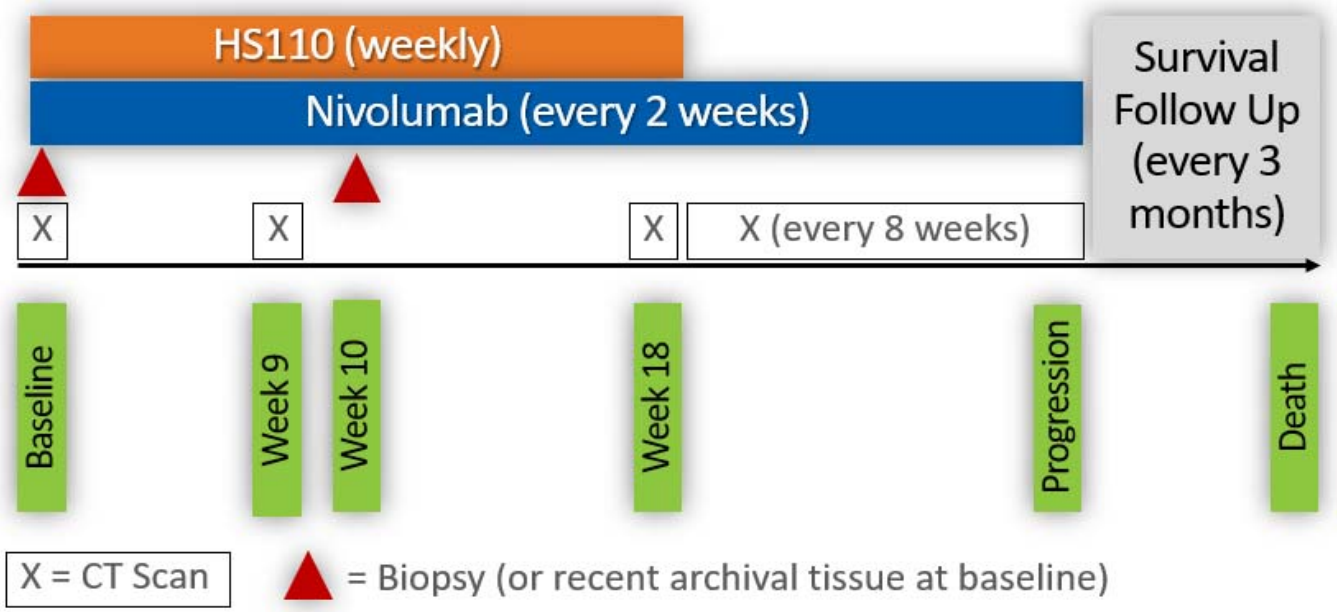
HS-110 Trial Schema

Cohorts A and B



Patients receive weekly HS-110 (1 x 10^7 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.

Clinical Proof-of-Concept Achieved

HS-110 in Combination with Nivolumab

Cohort A: 2+ line Checkpoint Inhibitor (CPI) naïve patients

Months	HS-110 + Nivolumab Δ 94% non-squamous and 6% squamous All (N=47)
Median PFS (95% CI)	1.84 (1.77, 7.75)
Median OS (95% CI)	**24.60 (11.70, 36.00) 29.7% still alive**

Months	Nivolumab Non-squamous BMS Checkmate 057 Study* (N=292)
Median PFS (95% CI)	2.3 (2.2, 3.3)
Median OS (95% CI)	**12.2 (9.7, 15.1)**

Δ Heat Biologics Cohort A interim results as of November 2020 data cut. Median follow-up time = 19.45 months. * Borghaei et al 2021. J Clin Oncol § Please note Heat Biologics' trial did not have a comparative nivolumab only arm. Published data in green is historical data and not HS-110 data.

Cohort B: 2+ line patients that progressed after CPI

Months	HS-110 + Nivolumab at ≥ 2nd line after CPI failure^ All (N=68)
Median PFS (95% CI)	2.76 (1.84, 3.91)
Median OS (95% CI)	**11.90 (9.72, 16.30) 26.5% still alive**

Months	Treatment Options at ≥ 3rd line after CPI failure		
	Gemcitabine† (N=27)	Docetaxel† (N=25)	Chemotherapy‡ (N=28)
Median PFS (95% CI)	2.8 (2.1, 3.4)	2.7 (2.0, 4.1)	4.7 (2.8, 7.0)
Median OS (95% CI)	**7.5 (3.0, 13.4)**	**6.8 (5.2, 11.5)**	**9.0 (7.7, 24.2)**

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- HS-110 in combination with nivolumab compares favorably with published data§
- Two 2+ line NSCLC settings are under evaluation:
  - 2+ line Checkpoint Inhibitor (CPI) naïve patients
  - 2+ line patients that progressed after CPI
- Potential registration strategies in combination with a PD-(L)1
  - Frontline treatment for NSCLC patients
  - NSCLC patients who progressed after prior PD-(L)1 treatment

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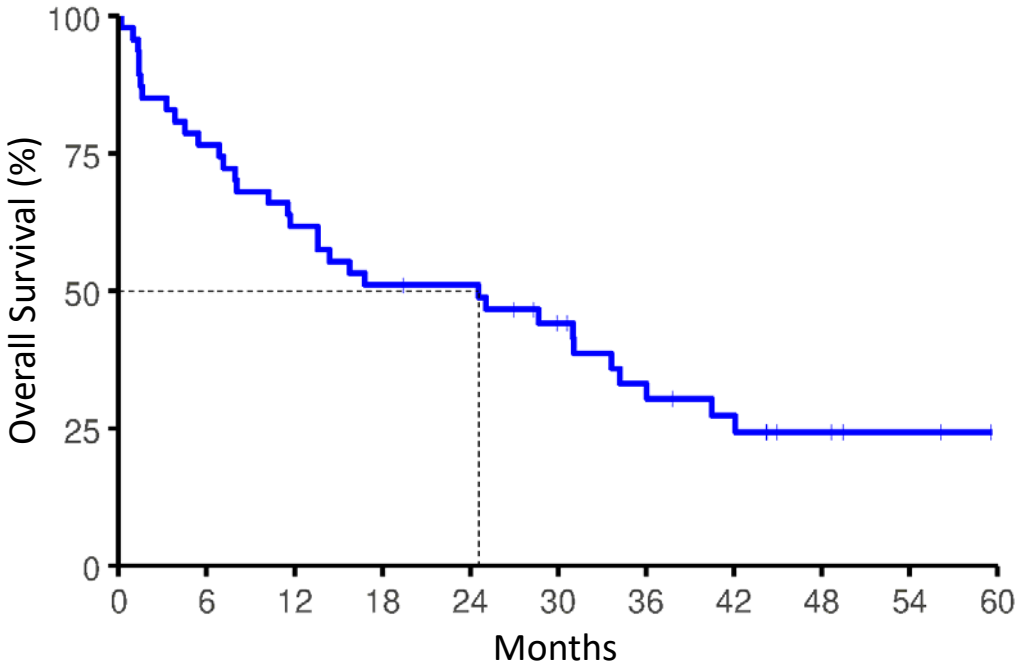
Cohort A:
CPI naïve pts treated by HS-110 + Nivolumab at ≥2L

Overall Survival (OS)



	HS-110 + Nivolumab Cohort A$^{\Delta}$
N	47
Median OS (95%CI)	24.60 (11.70, 36.00)
1-yr OS	61.70%

	Nivolumab§ BMS CheckMate 057 Study*
N	292
Median OS (95%CI)	12.2 (9.7 - 15.1)
1-yr OS	50.7%

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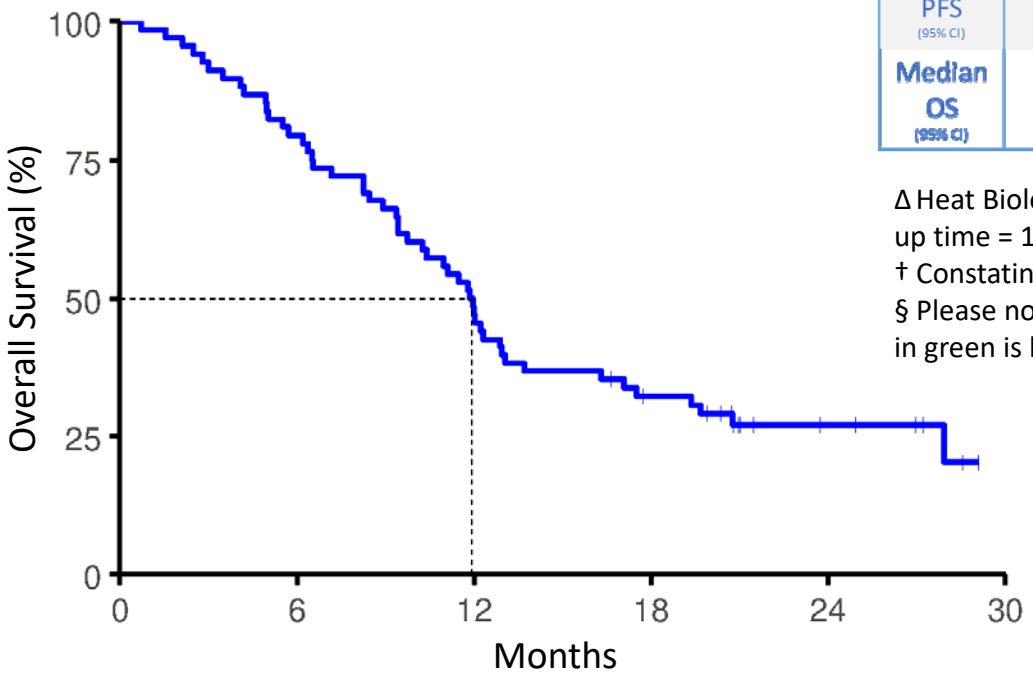
Cohort B:
CPI progressors treated by HS-110 + Nivolumab at ≥2L

Overall Survival (OS)



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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
- **Mechanism of action offers broad market potential**
- **Phase 1 in solid tumors currently enrolling**
- **Heat Biologics has worldwide rights**

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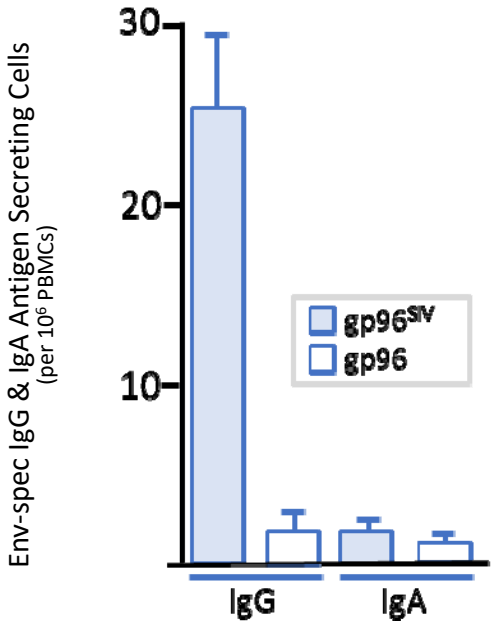
gp96 Platform for Infectious Disease

- gp96 platform demonstrated activity in animal models in multiple infectious diseases
  - Significant mucosal protection against simian immunodeficiency virus (SIV) in non-human primates
  - Induction of Zika-specific CD8+ T cells in mouse
    - No pathological changes in placenta or fetus
  - Elevation of malaria-specific CD8+ T cells in mouse
- Multiple grants received to utilize gp96 platform for various infectious diseases
  - National Institute of Health (NIH)
  - Department of Defense (DoD)
  - Florida Department of Health
- Heat Biologics leverages the body of work done to date to develop our COVID-19 vaccine program

Reference:
Strbo et al 2013 J Immunol. 2013 March 15; 190(6): 2495–2499
Strbo et al 2016 J Immunol May 1, 2016, 196 (1 Supplement) 146.10
Strbo et al 2018 J Immunol May 1, 2018, 200 (1 Supplement) 180.19

Induction of Humoral Immune Response by gp96^{SIV}Ig Vaccines



Key Differentiation of gp96 Platform

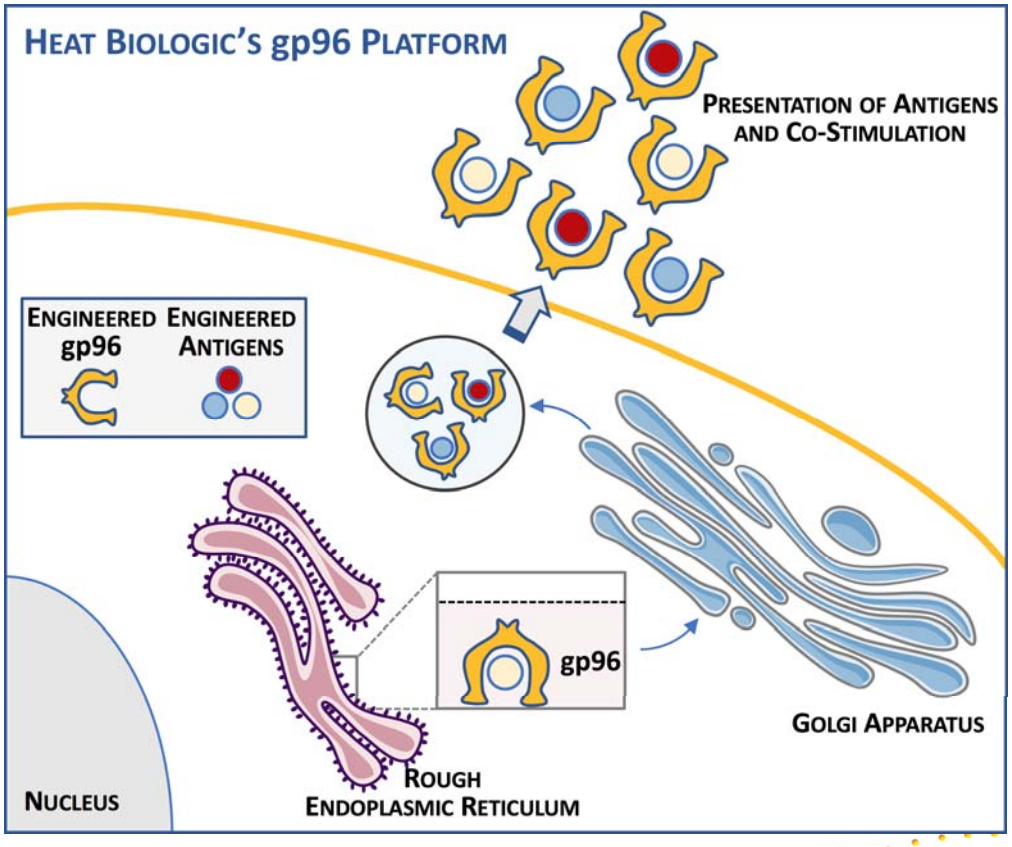
	gp96 Platform*
No Anti-Vector Immunity	✓
No Viral Activation	✓
No Integration of Foreign DNA into Host Genome	✓
Activation of T Cells	✓
Activation of B Cells	✓
High Immunogenicity	✓
Induction of Mucosal Immunity	✓
Long-Term Memory Response	✓

*Target product profile for infectious disease

- Heat's gp96 platform-based products evaluated in 250+ patients to date
  - HS-110 (Phase 2) demonstrated favorable safety profile and clinical activity in combination with PD-1 inhibitors for treatment of NSCLC
- Potential first-in-class for infectious disease
  - Based on human cells engineered to secrete gp96-bound antigens
    - Platform designed to be antigen-specific and pathogen-specific
  - Aim to activate both B and T cell responses at the point of pathogen entry
  - Preclinical work using gp96 platform includes SIV/ HIV, malaria and zika
- Heat's COVID-19 vaccine program utilizes the gp96 platform
  - Leverages natural immune process to induce long-lasting memory responses

Heat Biologics' COVID-19 Vaccine Program

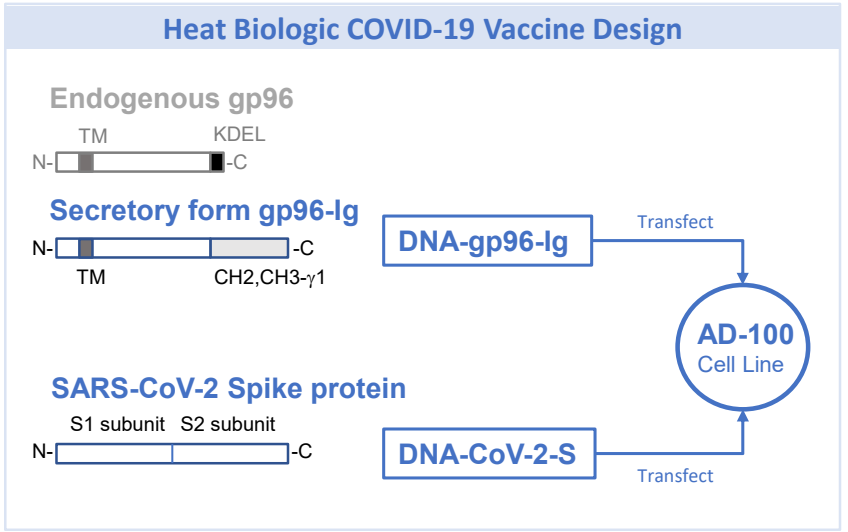
- Leverages our proprietary gp96 platform to activate the immune system
- Designed to elicit long-lasting immune response against SARS-CoV-2 virus
- We plan to collaborate with companies, researchers, government agencies and funding organizations to accelerate our COVID-19 vaccine program

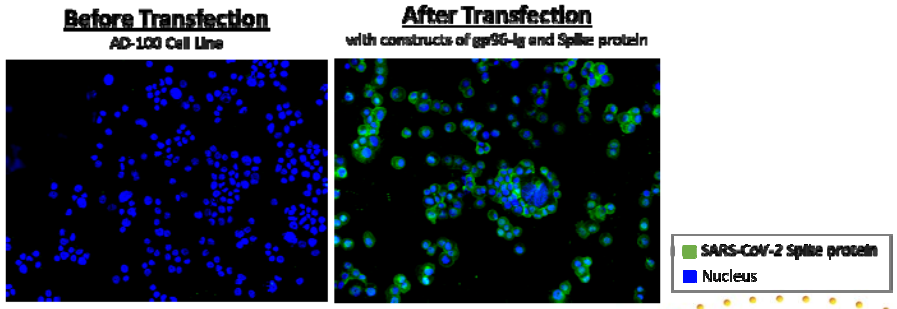


Heat Biologics COVID-19 Vaccine Program

Summary of Preclinical Data To Date

- Heat Biologics' COVID-19 vaccine utilizes gp96 technology and incorporates full length Spike protein
- Preclinical data demonstrated polyfunctional, polyepitope Spike protein-specific T cell responses as well as memory responses
- IND-enabling activities in progress





Fisher et al 2021. Front. Immunol. https://doi.org/10.3389/fimmu.2020.602254

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PTX-35 Overview

- **Potential first-in-class T cell co-stimulator targeting TNFRSF25, with preferential specificity to expand antigen-specific "memory" CD8+ T cells**
  - Phase 1 trial in solid tumors currently enrolling
- **Broad market potential**
  - Activity demonstrated in multiple preclinical *in vivo* colon, lung and breast cancer models
- **Synergistic combination with immunotherapies including HS-110 and checkpoint inhibitors**
- **Awarded a $15.2M grant to fund Phase 1 clinical development**
- **Worldwide rights licensed by Heat Biologics**

Synergy between anti-PD-(L)1 and TNFRSF25 Agonism

In Combination with Antigen-driven Immunotherapy

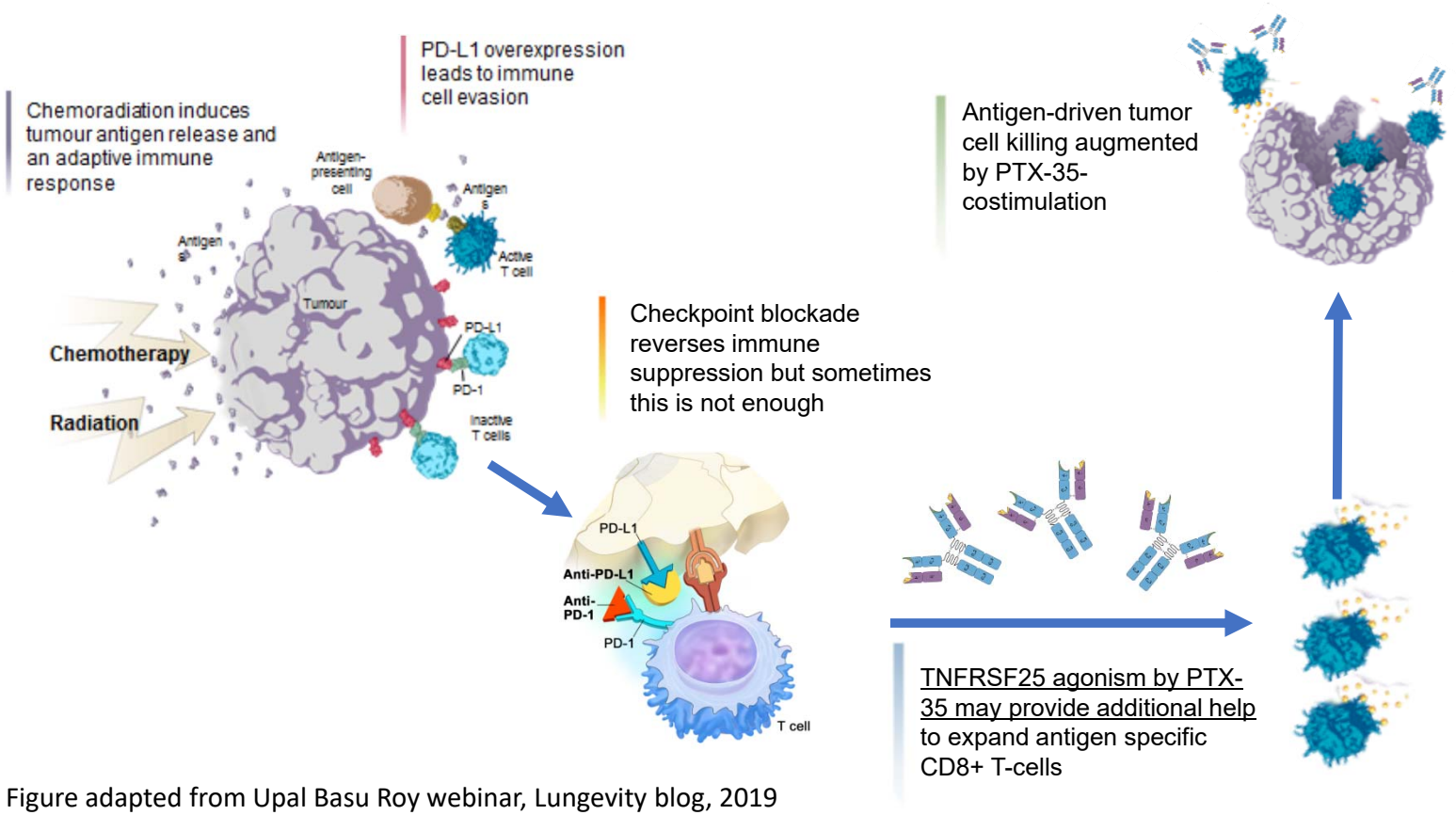

Figure adapted from Upal Basu Roy webinar, Lungevity blog, 2019

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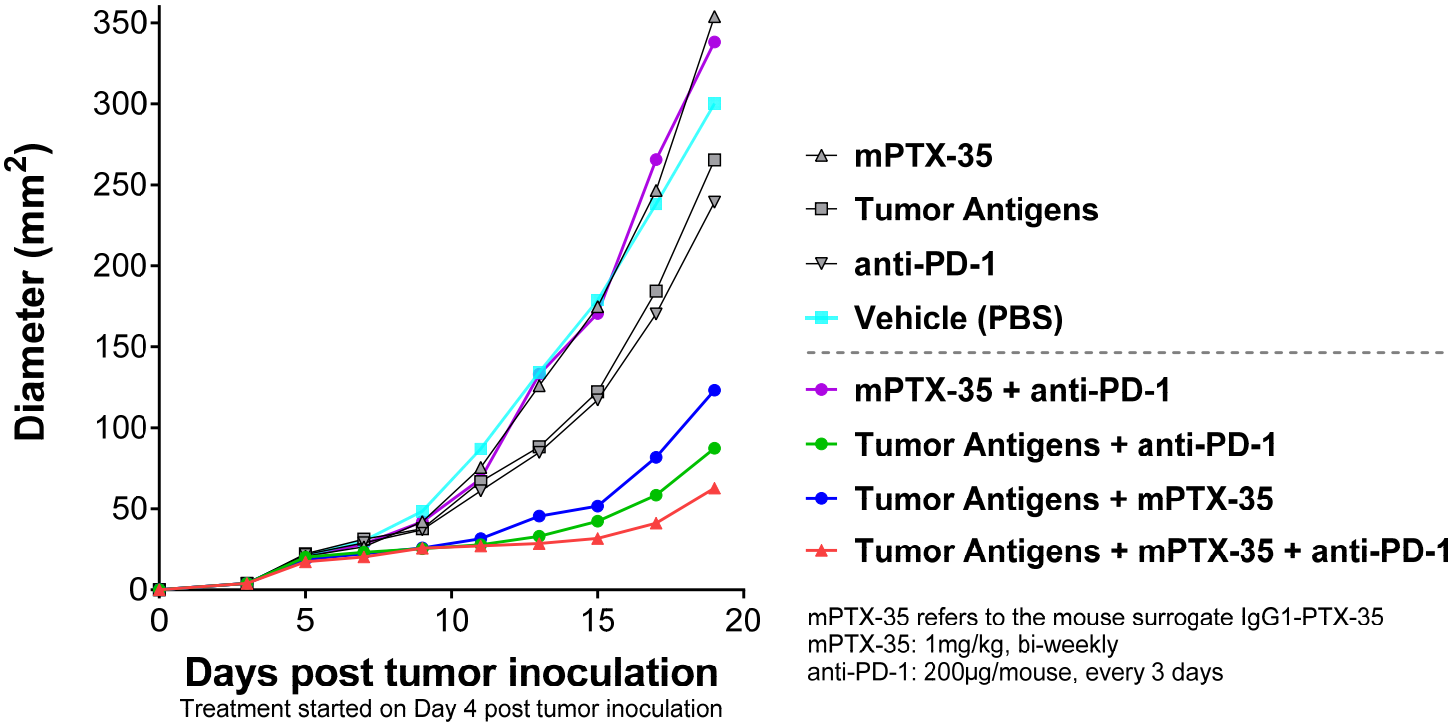
PTX-35 Demonstrated Anti-Tumor Activities

Synergy with Checkpoint Inhibition and Antigen-driven Immunotherapies

- Tumor growth inhibition (therapeutic setting)
  - Antigen is required for synergy between PTX-35 and anti-PD-1 inhibitor



mPTX-35 refers to the mouse surrogate IgG1-PTX-35
mPTX-35: 1mg/kg, bi-weekly
anti-PD-1: 200µg/mouse, every 3 days

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PTX-35: Key Nonclinical Data in Oncology

- **Activity demonstrated in multiple tumor models and in combination with checkpoint blockade and antigen-driven immunotherapies in mice**
  - PTX-35 has nanomolar potency
    - Agonist for TNFRSF25 for stimulating expansion of antigen-experienced T effector cells
  - *In vivo* pharmacodynamic activity as low as 10 µg/kg in mice
- **Favorable safety profile**
  - NOAEL = 100 mg/kg in monkeys and 200 mg/kg in mouse
  - No deleterious cytokine release in mouse, monkey and *in vitro* human cells
    - Conventional and regulatory T-cell expansion achieved
- **PTX-35 offers a unique opportunity to modulate an important target to expand conventional or regulatory T-cells**
  - Context driven depending on specific disease settings
  - Broad applications in cancer and autoimmunity

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