Heat Biologics

NASDAQ: HTBX

BIO CEO & INVESTOR CONFERENCE

FEBRUARY 2021

Forward Looking Statements

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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**

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Product Pipeline

Product	MOA (Modality)	Indication	Preclinical	Phase 1	Phase 2	Phase 3
HS-110	gp96 + CTAs (Cell Therapy)	NSCLC				
HS-130	OX40L (Cell Therapy)	Solid Tumors				
COVID-19 Vaccine	gp96 + Viral Antigens (Cell Therapy)	COVID-19				
PTX-35	TNFRSF25 (mAb)	Solid Tumors				

CTA = cancer testis antigen; NSCLC = Non-small cell lung cancer

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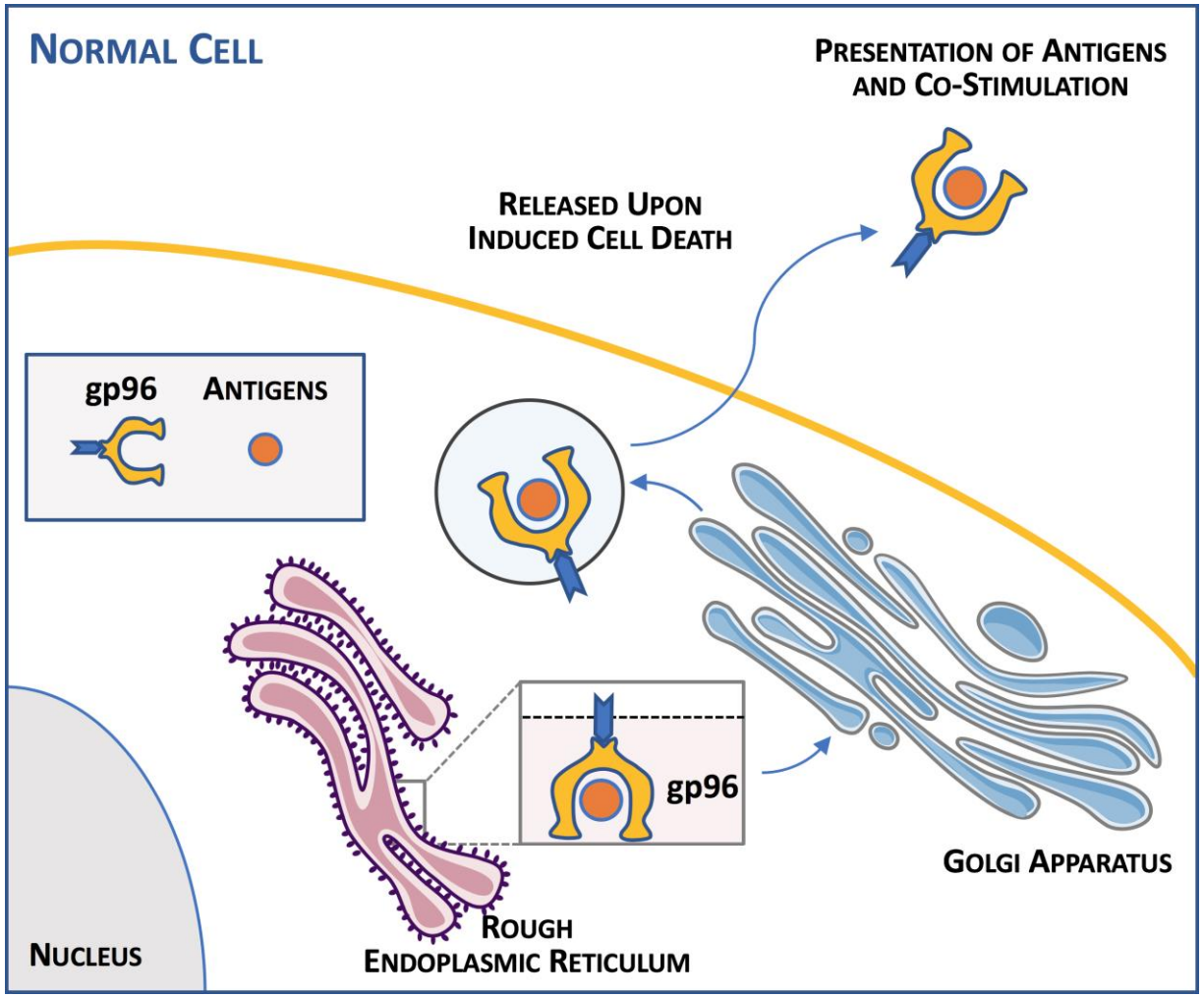
Heat Biologics' gp96 Platform

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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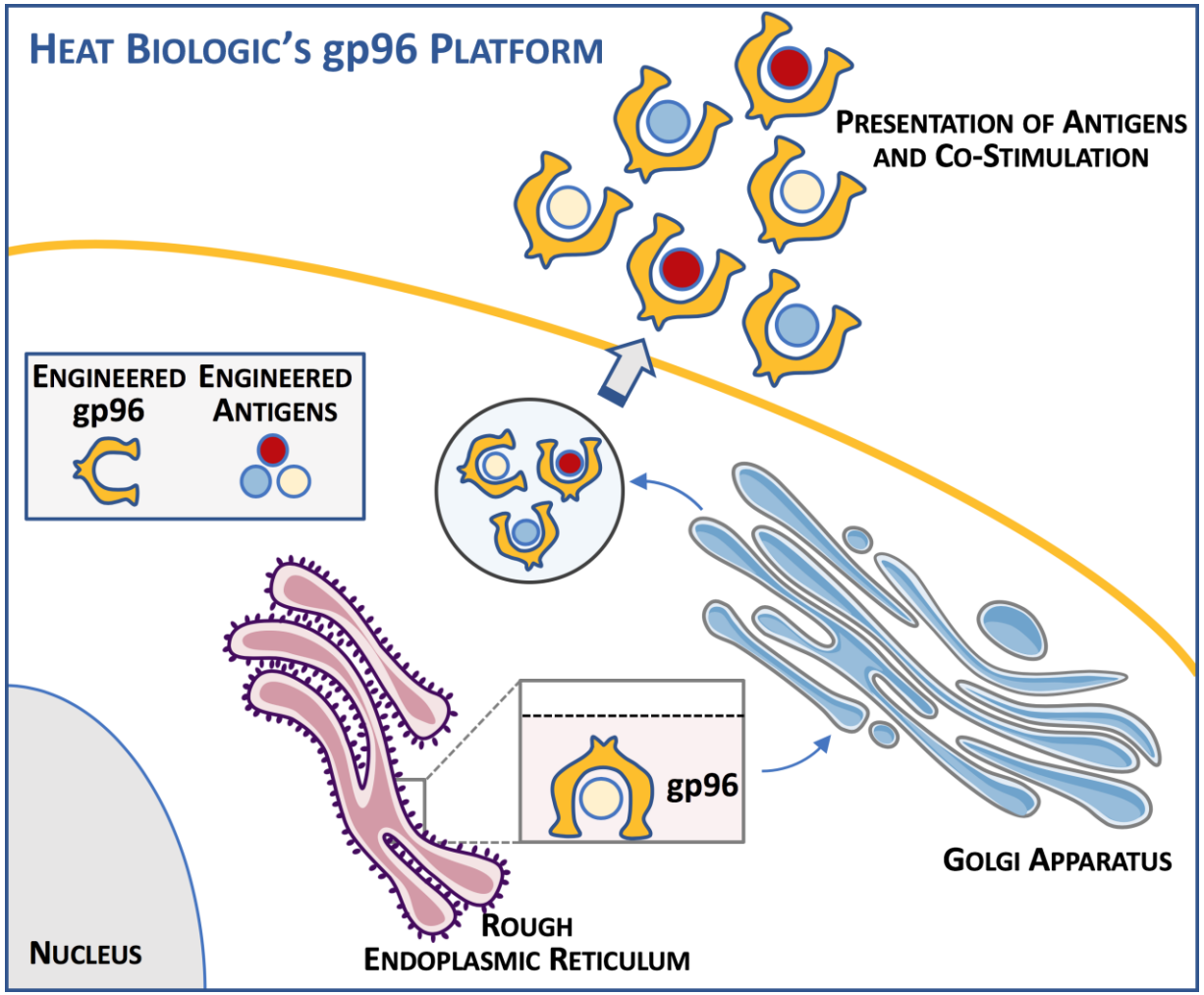

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  - Chaperones antigens (pathogens or tumor) to the immune system
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- Key features of Heat's gp96 platform
  - Leverages gp96's role as a natural molecular warning system
    - Engineered to secrete 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

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

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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	1.84
Median OS	24.60 29.7% still alive

Months	Nivolumab Non-squamous BMS Checkmate 057 Study* (N=292)
Median PFS	2.3
Median OS	12.2

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 Δ All (N=68)
Median PFS	2.76
Median OS	11.90 26.5% still alive

Months	Treatment Options at ≥ 3rd line after CPI failure		
	Gemcitabine† (N=27)	Docetaxel† (N=25)	Chemotherapy‡ (N=28)
Median PFS	2.8	2.7	4.7
Median OS	7.5	6.8	9.0

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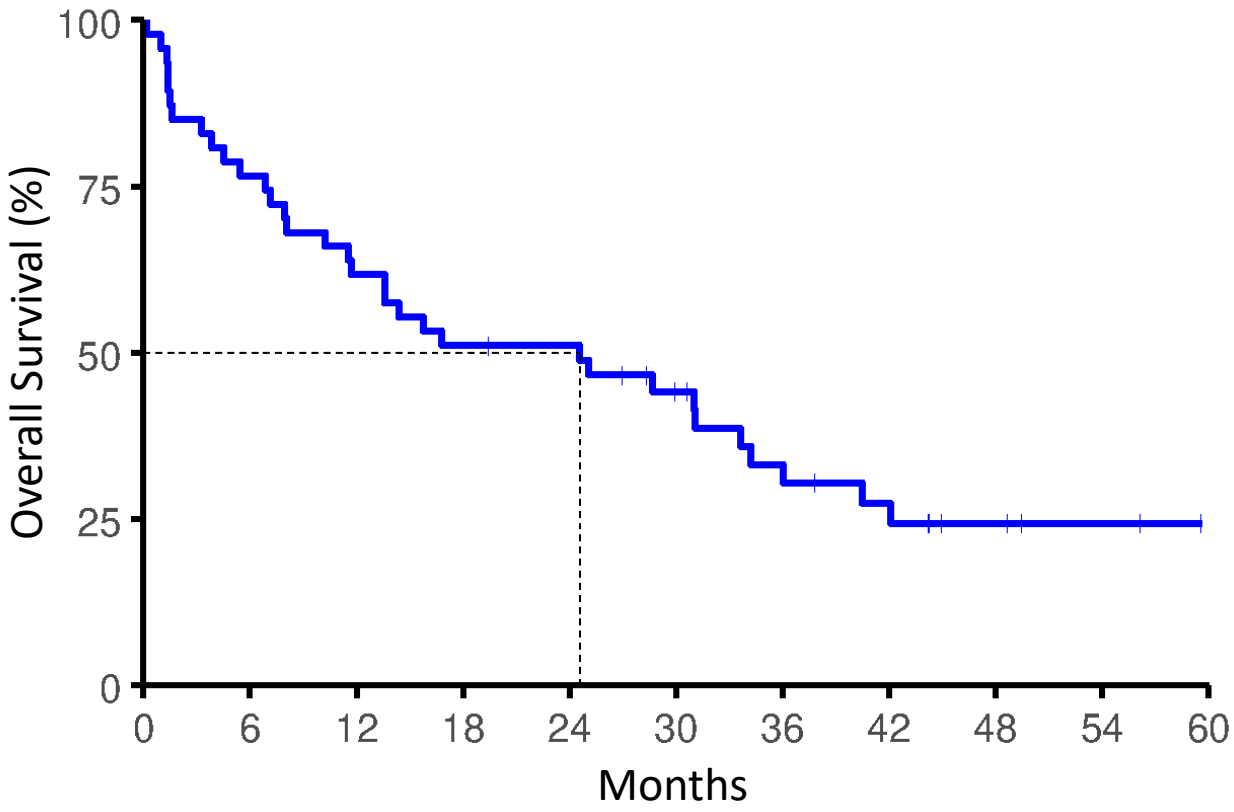
Cohort A:
CPI naïve pts treated by HS-110 + Nivolumab at ≥2L

Overall Survival (OS)



	HS-110 + Nivolumab
	Cohort A$^{\Delta}$
N	47
Median OS	24.60
1-yr OS	61.70%

	Nivolumab§
	BMS CheckMate 057 Study*
N	292
Median OS	12.2
1-yr OS	50.7%

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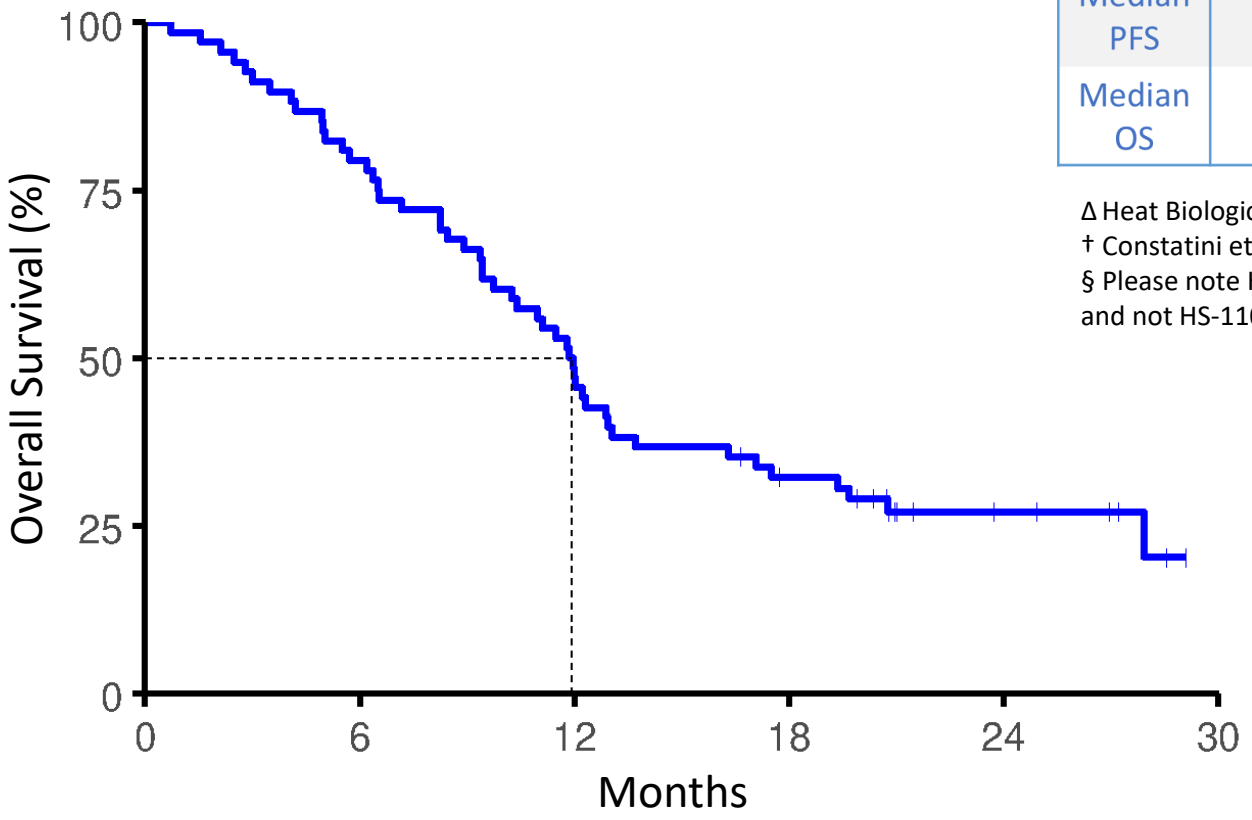
Cohort B:
CPI progressors treated by HS-110 + Nivolumab at ≥2L

Overall Survival (OS)



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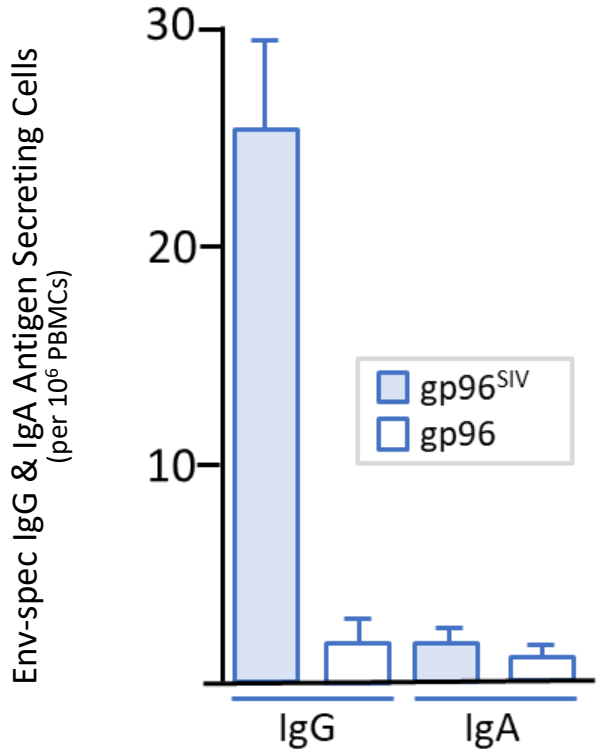
gp96 Platform for Infectious Disease

- 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



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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

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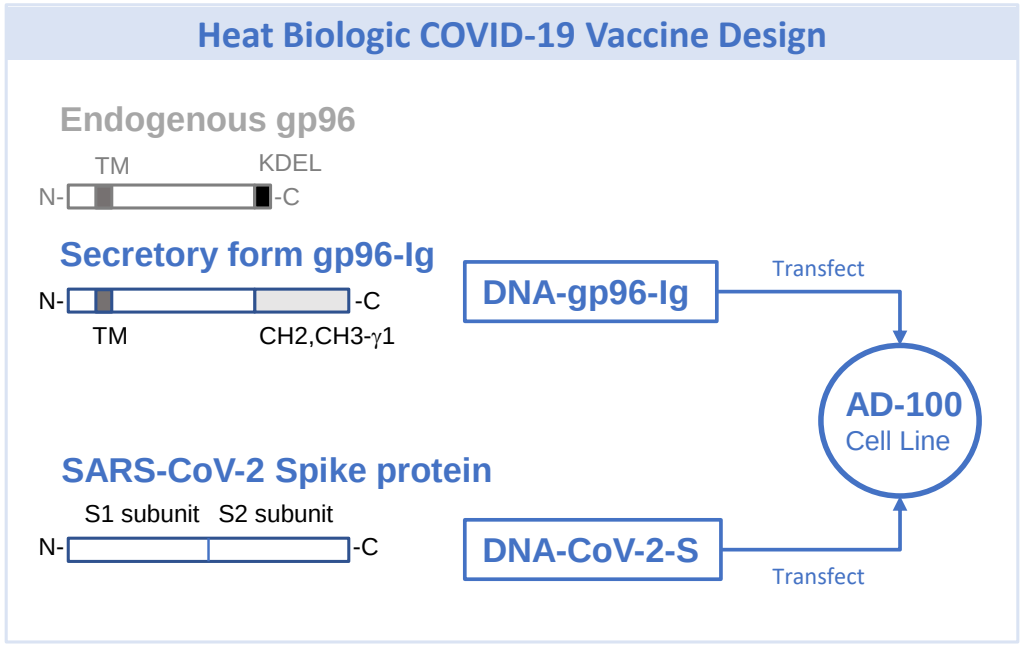
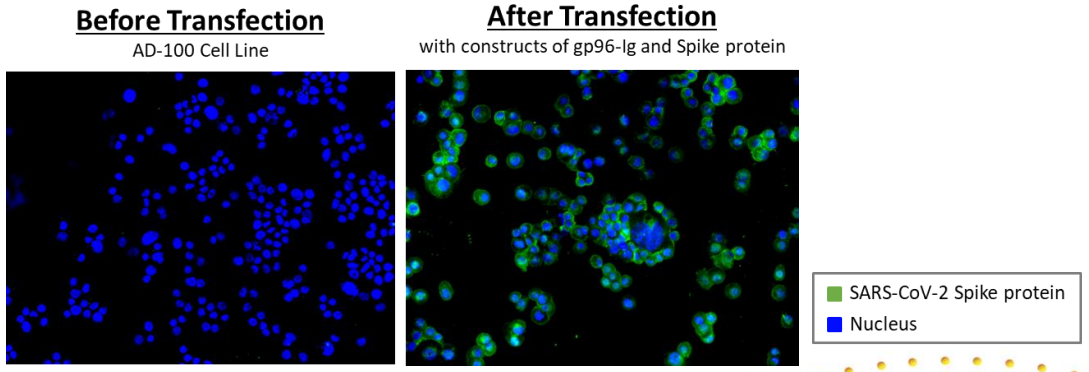
Heat Biologics COVID-19 Vaccine Program

Summary of Preclinical Data To Date

- Heat Biologics' COVID-19 vaccine leverages our proprietary gp96 platform to activate the immune system
- Designed to elicit long-lasting immune response against SARS-CoV-2 virus 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**
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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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