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, the proposed merger with Elusys Therapeutics, Inc., regarding timing of such merger, our ongoing and planned discovery and development of drugs targeting cancer, non-oncology and infectious diseases, our planned discovery and development of a COVID-19 vaccine, our planned biosecurity/biodefense initiative, our planned bioanalytics, process development and manufacturing activities, our biologics drug discovery, 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, 2020, 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)
Headquarters: Research Triangle Park, NC

Fully integrated biopharmaceutical company focused on developing first-in-class immunotherapies
- Well-capitalized with strong balance sheet - over $108M* in cash and cash equivalents

Planned acquisition of Elusys Therapeutics
- Developer and marketer of FDA, Canada, EU and UK approved Anthim® (obiltoxaximab), best-in-class antitoxin for anthrax
- Received over $320M in US government development and procurement contracts

Major programs include:
- HS-110, “off-the-shelf” cell-based immunotherapy - Positive Phase 2 results in NSCLC
- PTX-35 first-in-class immunomodulatory antibody - Phase 1 trial in solid tumors ongoing
- RapidVax® - novel cell-based vaccine platform designed to accelerate time to clinic for targeting emerging biological threats

Heat’s subsidiary ecosystem enables end-to-end development from bench to clinic

Unique proprietary biologics drug discovery platform to accelerate novel target identification

Biologics manufacturing, immunoassays, cell-based assays, and biomarker support

*Sep 30, 2021
Elusys Therapeutics
Biodefense and Pandemic Preparedness Subsidiary

Definitive agreement for acquisition executed in December 2021
- Sophisticated knowledge and hands-on experience in biodefense biologics manufacturing
- Program Management expertise with government agencies including the NIH, DoD, and BARDA

Developer and marketer of Anthim®, best-in-class monoclonal antibody antitoxin for anthrax
- FDA approval (treatment and prophylaxis) in 2016 and US orphan drug designation
- Approved in 2020 as only licensed anthrax treatment in EU and UK
- Orphan drug designation in EU at time of approval (10 years)

Established government partnerships and funding
- Received over $250M of non-dilutive development contracts from the NIH, DoD, and BARDA
- Completed 2 delivery orders totaling $70M in procurement contracts to supply Anthim to the U.S. Strategic National Stockpile (SNS) (2016, 2018)
Skunkworx Bio (subsidiary of Heat Biologics) is focused on biologics drug discovery using a proprietary platform to enable rapid drug development

- Accelerated program designated for advancing leads from discovery into preclinical development

Unique Hotspot Approach and Proprietary Pocket Biologics

- Uses advanced computational methods and bioinformatics to aid in development of next-generation precision therapeutics
- Novel, highly diverse, and proprietary compound libraries being used to identify small proteins and human antibodies which bind to critical druggable targets involved in protein-to-protein interactions

Located in the New Jersey Bioscience Center, a highly selective bioscience incubator in the heart of New Jersey’s “Research Corridor”
Scorpion Biological Services (subsidiary of Heat Biologics) is designed to provide scale-up manufacturing, biomarker, companion diagnostics and assay development

- Aims to accelerate Heat’s product development efforts from discovery to clinical development
- Offers contract manufacturing and bioanalytical services to biopharmaceutical companies

**Biologics Manufacturing**

- Designed to provide a scalable process development and production of GMP material through to large-scale manufacturing and cold storage facilities

**Bioanalytical and Diagnostic Services**

- Immuno-Assay (ELISA, Flow Cytometry, ELISPOT/FluoroSpot, qPCR, MagPix)
- Cell-based assays (method development, qualification, validation)
- Biomarker support (Luminex, IsoPlex, ELISA)
- Potential to expand into a CLIA-regulated facility for companion diagnostics
Heat Biologics subsidiary ecosystem enables end-to-end solution for efficient clinical development

- Skunkworx Bio: Utilizes a unique proprietary biologics drug discovery platform to accelerate novel target identification
- Scorpion Biological Services: Large molecule CRO focused on immunoassays, cell-based assays, and biomarker support
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* Pending acquisition of Elusys Therapeutics

CTA = cancer testis antigen
NSCLC = Non-small cell lung cancer
Heat Biologics’ gp96 Platform
Activating the Immune System

Function of heat shock protein gp96
- Potent mucosal adaptive memory inducer
- Chaperones antigens (pathogen or tumor derived) to antigen presenting cells to promote 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
- Can be engineered to secrete target antigens bound to gp96-Ig
- Off-the-shelf allogeneic cell vaccine
- Feasible for large scale manufacturing
- Amenable to stockpiling
- Broad applications in infectious diseases and cancer

Lead product completed Phase 2 trial for NSCLC
HS-110 Overview

**gp96-Based Cancer Vaccine Targeting Solid Tumors**

**HS-110** is a first-in-class, “off-the-shelf”, allogeneic cell-based immunotherapy

- Designed to secrete multiple cancer testis antigens chaperoned by heat shock protein gp96, to co-stimulate antigen presenting cells and to expand tumor antigen-specific T cells
- Broad potential for providing multiple treatment options to NSCLC patients in combination with a PD-1 inhibitor
- Worldwide rights available

**Clinical proof-of-concept in combination with PD-1 therapy for multiple treatment settings of NSCLC**

- Enrollment for Phase 2 NSCLC trial (n=122) complete
- Positive interim survival data demonstrated in previously treated PD-(L)1 naïve and PD-(L)1 progressor NSCLC patients
- Plan to discuss Phase 3 registrational pathways with FDA as well as potential partners

**Combination of HS-110 and PD-(L)1 therapies may confer additional survival benefit in multiple cancers**

- Line extension strategy to include additional indications that have been approved for PD-(L)1 therapies
HS-110 is designed to utilize gp96 to
- Chaperon multiple CTAs for effective update by antigen presenting cells via CD91
- Activate antigen presenting cells via stimulation of toll-like receptor (TLR)-2 and TLR-4
- Activate & expand antigen-specific cytotoxic CD8+ T cells

Synergistic combination of HS-110 and anti-PD-1 inhibitor demonstrated
- Preclinical anti-tumor activity in multiple cancer models
- Clinical proof-of-concept in multiple settings of NSCLC
**HS-110 Phase 2 Trial Schema**

**Checkpoint Inhibitor Naïve (Cohort A) and Progressor (Cohort B) Patients**

**Patients:**
- Previously treated adult patients with unresectable or with adenocarcinoma or squamous NSCLC
- ≥ 1 lesion measurable by RECIST 1.1
- ECPG PS 0 or 1

**Cohort A:**
Checkpoint Inhibitor naïve patients (n=47)

**Cohort B:**
Checkpoint Inhibitor progressor patients (n=68)

**Baseline**

<table>
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<th>Week 9</th>
<th>Week 10</th>
<th>Week 18</th>
<th>Progression</th>
<th>Death</th>
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**Primary Outcome:** ORR (per RECIST 1.1)

**Key Secondary Outcome:**
PRS (per RECIST 1.1), OS, Safety and tolerability

**Retrospective subgroup analyses:**
- Injection site reaction (yes vs. no)
- Baseline bTMB (<10 vs. ≥10 mut/Mb)
- Baseline PD-L1 expression (<1% vs. ≥1%)

bTMB, baseline blood tumor mutational burden; ID, intradermal; ISR, injection-site reaction; IV, intravenous; mut/Mb, mutations per megabase;
HS-110 Clinical Proof-of-Concept Achieved

**HS-110 in Combination with Nivolumab**

| **Cohort A: Previously treated Checkpoint Inhibitor (CPI) naïve NSCLC patients** |
|----------------------------------|---|---|
| **HS-110 + Nivolumab**<sup>a</sup> | 94% non-responders and 6% responders |
| All (N=47) | ISR+ (N=20) | PD-L1+ (N=9) |
| OS (mos) | 24.6 (11.7, 36.0) | 36.0 (28.7, NE) | 40.5 (8.0, NE) |
| **Nivolumab** | Non-responders | BMS Checkmate 057 Study<sup>*</sup> |
| OS (mos) | 12.2 (9.7, 15.1) |

<sup>a</sup> Heat Biologics Cohort A interim results as of November 2020 data cut. Median follow-up time = 10.4 months. Subgroup analyses were retrospective.

<sup>*</sup> Borgna 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. Injection site reaction (ISR), yes (+) or no (-), and baseline PD-L1 expression, – (<1%) or + (≥1%).

| **Cohort B: NSCLC patients whose disease had progressed on or after prior CPI treatment** |
|----------------------------------|---|---|---|
| **HS-110 + Nivolumab** at 2nd line after CPI failure<sup>a</sup> | 12.1 (11.1, 20.8) | 18.2 (12.9, NE) | 12.0 (9.4, NE) |
| All (N=50) | ISR+ (N=52) | bTMB-L (N=32) | PD-L1+ (N=23) |
| OS (mos) | 11.9 (9.7, 16.3) | 26.5% still alive | 12.1 (11.1, 20.8) | 18.2 (12.9, NE) | 12.0 (9.4, NE) |

<sup>a</sup> Heat Biologics Cohort B interim results as of November 2020 data cut. Median follow-up time = 11.9 months. Subgroup analyses were retrospective.

| **Treatment Options** at 3rd line after CPI failure |
|----------------------------------|---|---|---|
| Gemcitabine<sup>f</sup> (N=27) | Docetaxel<sup>f</sup> (N=25) | Chemotherapy<sup>f</sup> (N=28) |
| OS (mos) | 7.5 (3.0, 13.4) | 6.8 (5.2, 11.5) | 9.0 (7.7, 24.2) |

<sup>f</sup> Constantini et al 2018 EU Open Research † Schwartzman et al 2017 Lung Cancer. § Please note Heat Biologics’ trial did not have a chemotherapy only arm. Published data in green is historical data and not HS-110 data. Injection site reaction (ISR), yes (+) or no (-), baseline blood tumor mutational burden (bTMB), bTMB-L (<10 mutations/ megabase [MB/m]b) or bTMB-H (>10 MB/m) by FoundationiCT test and baseline PD-L1 expression, – (<1%) or + (≥1%).

**HS-110 in combination with nivolumab compares favorably with published data<sup>§</sup>**
- Combination of HS-110 / nivolumab well-tolerated

**Two 2L+ NSCLC settings are under evaluation**
- 2L+ Checkpoint Inhibitor (CPI) naïve patients
- 2L+ patients that progressed after CPI treatment

**Potential strategy to accelerate clinical development**
- Improved OS in subsets of patients with injection site reaction (ISR)
PTX-35 Overview
Potential First-in-Class TNF Receptor Superfamily Member Death Receptor 3 (TNFRSF25/DR3) Agonist Antibody

PTX-35 offers a unique opportunity to modulate T effector or regulatory T-cells
- PTX-35 is an immunomodulatory co-stimulator of DR3
- Context driven depending on specific disease settings
- Broad applications in oncology and non-oncology
- Favorable safety profile demonstrated in mice and non-human primates

Phase 1 trial in solid tumor trial currently enrolling
- Anti-tumor activity demonstrated in multiple preclinical in vivo colon, lung and breast cancer models
- Preclinical data demonstrate anti-tumor activity, expansion of antigen-specific CD8\(^+\) T cells and decreased Treg suppression in the presence of tumor antigen (AACR 2021)
- Awarded a $15.2M CPRIT grant to fund Phase 1 clinical development

Worldwide rights licensed by Heat Biologics
Mechanism of Action PTX-35
Immunomodulatory Activity Dependent on Presence or Absence of Danger Signal

TNFRSF25/DR3
- Highly and constitutively expressed on CD4+ FoxP3+ regulatory T cells (Treg)
- Minimally expressed on non-activated CD8+ T cells

In the absence of a danger signal, co-stimulation of DR3 promotes
- Selective expansion of functional Tregs that can suppress inflammation
- Increased expression of immunosuppressive markers including CTLA4, TIGIT, and PD-1
- Minimal impact on resting CD4+ and CD8+ T cells

In the presence of a danger signal (activating) that can arise from infection or cancer, co-stimulation of DR3 promotes
- Enhanced expansion of activated CD8+ effector T cells
- Increased percentage of inflammatory IFNγ+ Th1 and IL-17+ Th17 CD4+ T cells
- Decreased functional CD4+ FoxP3+ Tregs characterized by reduced CTLA4 expression
Anthim® Overview
Best-in-Class Antitoxin for the Treatment of Anthrax

Anthim treats & protects against inhalational anthrax disease
- Monoclonal antibody that binds protective antigen (PA83) released by *bacillus anthracis*
- Neutralizes anthrax toxin
- Treatment in combination with antibiotics or prophylaxis when alternative therapies are not available
- For complete prescribing information including limitations of use and box safety warning associated with HYPERSENSITIVITY and ANAPHYLAXIS, see www.Anthim.com

US FDA approval in 2016; Canada, EU and UK approval as of 2020
- Only anthrax antitoxin to have received international licensure

Higher affinity than competitor *

Anthim is supplied to the US Strategic National Stockpile
- As part of ASPR’s objective to diversify supply and acquire products with a longer shelf-life, completed and shipped 2 orders totaling $70M in 2016 and 2018

*Per product package inserts
Image courtesy of CDC
Mechanism of Action Anthim®
Anthim Binds Protective Antigen to Prevent Anthrax Toxin Receptor Interaction

**Bacterium Releases Anthrax Toxin Subunits**
- Protective Antigen (PA83)
- PA20
- PA63
  - Lethal Factor (LF)
  - Edema Toxin (ET)

**PA83 Binds to Host Cell ATR & is Cleaved by Furin to PA63**
- PA83
- ATR
- PA20
- PA63
- PA63 Heptamer

**Bound PA63 Forms a Heptamer**
- Lethal Factor (LF)
- Edema Toxin (ET)

**PA63 Binds LT and ET Leading to Endocytosis, Edema, and Cell Death**
- Lethal Factor (LF)
- Edema Toxin (ET)

**Anthim Binds to PA83 and Inhibits ATR Binding**

*ANTHRAX TOXIN MEDIATED CELL DEATH AND EDEMA*
Novel “plug-and-play” allogeneic cellular vaccine platform

- Utilizes premanufactured gp96-Ig/OX40L-Ig expressing stockpile-amenable cells
- Leverages Heat’s vast experience with gp96-based vaccines including a favorable safety profile in over 250 oncology patients
- Enables target antigen sequences to be transfected into premanufactured RapidVax cells to rapidly create a pathogen-specific prophylactic vaccine upon identification of emerging biological threats
- Potential to dramatically reduce time from identification to immunization

Images courtesy of CDC, National Genome Research Institute, NIH
Mechanism of Action RapidVax®
Potential to Stimulate Pathogen-Specific Cellular and Humoral Immunity

1. Pathogen Target Antigen(s) are identified and expressed in RapidVax Base Cells

2. Expressed Antigen(s) are chaperoned to APCs by TLR2/4 Stimulating gp96-ig

3. APCs process and display pathogen antigen(s) to activate cognate T cells

4. Co-stimulatory OX40L-ig released by RapidVax supports the generation of memory T cells (T_{mem}) and the expansion of T follicular helper (T_{fh}) cells

5. Cytotoxic T cells target infected cells while T_{reg} cells support B cell antibody production

RapidVax
- Engineered gp96-ig
- OX40L-ig
- Target Antigen(s)
- Pathogen
- Antibody
Biological Threat Advisory Board of Heat Biologics
Bipartisan Board Providing Counsel on Heat’s Biodefense and Pandemic Preparedness Initiatives

David Lasseter
Former Deputy Asst. Sec. of Defense for Countering Weapons of Mass Destruction

Andrew Weber
Former Asst. Sec. of Defense for Nuclear, Chemical & Biological Defense Programs

Jack Kingston
Former US Representative, Secretariat of the Alliance for Biosecurity (current)

Dr. Gregory Koblentz
Professor of Biodefense at George Mason University, Expert on Chemical and Biological Weapons

Mark Pryor
Former US Senator, AR
Heat Biologics Highlights

Robust immunotherapy pipeline spanning oncology, non-oncology and infectious disease indications
• Multiple biologics advanced from bench to clinic
  - HS-110 (allogenic cell therapy)
  - HS-130 (allogenic cell therapy)
  - PTX-35 (antibody-based therapy) - $15.2M CPRIT grant to advance clinical development

End-to-end accelerated capabilities from discovery to manufacturing to clinical trial
• Skunkworx discovery subsidiary unique proprietary biologics drug discovery platform accelerates novel target identification
• Newly established Scorpion Biological Services subsidiary to provide process development, cGMP manufacturing, analytical test methods development and cGMP testing services

Expanding biodefense and pandemic preparedness portfolio
• Planned acquisition of Elusys Therapeutics – developer and marketer of Anthim® (obiltoxaximab), best-in-class antitoxin for anthrax
• Received over $320M in development and procurement contracts to support Anthim
• RapidVax® cellular vaccine platform in development to accelerate time to clinic from pathogen identification to immunization
• Bipartisan Biothreat Advisory Board provides guidance on Heat’s biodefense and pandemic preparedness initiatives