**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): **April 1, 2019**

# Heat Biologics, Inc.

*(Exact name of registrant as specified in charter)*

**Delaware**
*(State or other jurisdiction of incorporation)*

| **001-35994** | **26-2844103** |
|---|---|
| *(Commission File Number)* | *(IRS Employer Identification No.)* |

**801 Capitola Drive**
**Durham, NC 27713**
*(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 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))

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 7.01 Regulation FD Disclosure.**

Heat Biologics, Inc. (the "Company") presented the information in the presentation poster attached hereto as Exhibit 99.1 at the American Association of Cancer Research Annual Meeting 2019 on April 1, 2019 in Atlanta, Georgia.

The furnishing of the attached presentation is not an admission as to the materiality of any information therein. The information contained in the poster is summary information that is intended to be considered in the context of more complete information included in the Company's filings with the Securities and Exchange Commission (the "SEC") and other public announcements that the Company has made and may make from time to time by press release or otherwise. The Company undertakes no duty or obligation to update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases or through other public disclosures.

The information in this Item 7.01 of this Current Report on Form 8-K and Exhibit 99.1 attached hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in any such filing.

**Item 8.01 Other Events.**

On April 2, 2019, the Company issued a press release announcing the presentation of an animal study that demonstrated the combination of mouse HS-110 and mouse HS-130 yielded a three-fold increase in anti-tumor CD8+ T-cell expansion in a poster presentation at the American Association of Cancer Research Annual Meeting 2019 on April 1, 2019 in Atlanta, Georgia. A copy of the press release regarding this presentation is attached as Exhibit 99.2 hereto and is incorporated herein by reference.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits.

| Exhibit Number | Description |
|---|---|
| 99.1 | Heat Biologics, Inc. poster presentation |
| 99.2 | Press Release of Heat Biologics, Inc. dated April 2, 2019 |

**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: April 2, 2019

HEAT BIOLOGICS, INC.

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

**EXHIBIT INDEX**

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| 99.1 | Heat Biologics, Inc. poster presentation |
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# Generation of a Novel, Allogeneic Cell-based, Gp96-Ig/OX40L Cancer Vaccine, Improves Anti-Tumor Immunity and Long-Term Memory T-cell Generation

Vikas Tahiliani, Jayalakshmi Miriyala, Patrick Dillon, Jason Rose, Louise Giffin, Jeff Hutchins, Matthew M Seavey*
Heat Biologics, Inc, Durham, NC, USA

Poster# 5744

## Abstract & Background

Heat Biologics' technology is focused on developing a next generation cellular vaccine that incorporates a tumor antigen chaperone (gp96-Ig) with T-cell costimulation (OX40L-Ig) into a single tumor cell line. Viagenpumatucel-L (HS-110; ImPACT), a human lung adenocarcinoma cell line, stably transfected to express gp96-Ig is being tested in a Phase 2 clinical trial (NCT#02439450) with checkpoint inhibition for NSCLC. A similar line is being generated that will complement HS-110, providing costimulation in the form of secreted OX40-Ig (HS-130). To model how the addition of human HS-130 to HS-110 may impact anti-tumor immune responses, we generated mouse surrogates of these human lines and established an analogous system that treats tumor-bearing animals with tissue-matched irradiated mouse cancer cell lines (melanoma; B16F10) expressing gp96-Ig (mHS-110) and OX40L-Ig (mHS-130); both expressing ovalbumin (OVA), as our model tumor-associated antigen. Single dose vaccination with mHS110 identified that 300 ng to 3000 ng of secreted gp96-Ig provided sufficient anti-tumor CD8+ T-cell expansion, with the greatest expansion observed on day 7, post-immunization. To identify the best ratio of mHS-110 to mHS-130; a dose ratio study was performed. Fixed numbers of mHS-110 (300 ng of secreted gp96-Ig) were matched with different ratios of mHS-130 (OX40L-Ig). Similar to our single dose vaccination study, our results demonstrated that the peak CD8+ T-cell expansion occurred on day 7 post-immunization, and that the addition of mHS-130 further boosted anti-tumor CD8+ T-cell expansion by 3-fold when the ratios of mHS-110 to mHS-130 were at a 1-to-0.5 ratio (300 ng of secreted gp96-Ig to 150 ng of secreted OX40L-Ig). These animals were subsequently boosted 14-days post-immunization, and we similarly found that the 1-to-0.5 ratio of mHS-110 to mHS-130 gave the maximum expansion of CD8+ T cell responses, peaking on days 19-21 and contracting thereafter. Importantly, these ratios led to higher frequencies of antigen-specific CD8+ T cells at both priming and boosting, which enhanced rejection of established B16F10 tumors and increased overall animal survival.

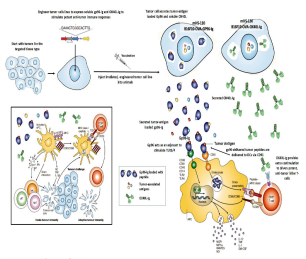

**Figure 1: Mechanism of Action**
Tissue-matched, allogeneic tumor lines are engineered to express soluble versions of heat-shock protein, gp96, and a potent costimulatory molecule, OX40L (HS-110 and HS-130, respectively). The KDEL endoplasmic reticulum retention sequence of gp96 was replaced by an IgG1 Fc chain. Since gp96 is responsible for folding endogenous proteins, many of which are destined for MHC-I loading; sequestered tumor peptides are delivered to antigen presenting cells (APCs) for CD8+ T-cell cross-presentation. Gp96 is a danger associated molecular pattern (DAMP) that stimulates inflammatory cascades via TLR2/4 stimulation and via uptake by scavenger receptor CD91. With the addition of a costimulatory molecule, OX40L fused with an IgG1 Fc chain, anti-tumor CD8+ T-cell responses are further enhanced. Activation of DCs by tumor-antigen loaded gp96 and costimulation by OX40L can enhance the innate and adaptive arms of immunity, via pro-inflammatory cytokines. *Figure adapted from Nechitila CV, Nature reviews Immunology, Vol-3, May 2003*

## Finding the Best Dosing Ratio to Predict Optimal Anti-Tumor Responses

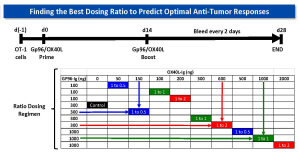


**Figure 2: Variable Ratio; Dose Escalation Study to Determine Optimum Anti-Tumor CD8+ T-cell Expansion**
T-cell receptor transgenic mouse CD8+ (OT-I) cells were isolated from in-house bred OT-I GFP mice using Easy Sep Mouse CD8+ T Cell isolation kit and injected into each C57BL/6 mouse intravenously (i.v) through lateral tail vein with 1 million OT-I cells suspended in HBSS. One day after injecting OT-I, all the mice were tail bled for baseline and 4 hours later, mHS-130 (B16F10-OVA-gp96-Ig) and mHS-130 (B16F10-OVA-OX40L-Ig) were treated with 10 µg/mL of Mitomycin-C for 3 hours and given intraperitoneally (i.p.) to each group accordingly. Animals were dosed based on nanogram expression level (determined by measuring the supernatants of culturing per 1 million cells in a 24 hour period) of gp96-Ig or OX40L-Ig.

## CD8+ T-cell Expansion Over Time with gp96/OX40L-Ig Prime & Boost

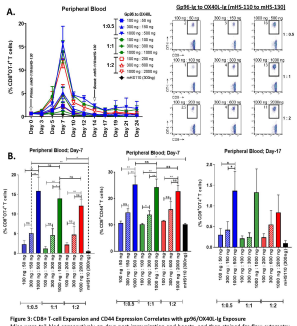


**Figure 3: CD8+ T-cell Expansion and CD44 Expression Correlates with gp96/OX40L-Ig Exposure**
Mice were tail bled consecutively on days post-immunization and boosts, and then stained for flow cytometry. **(A)** Graph shows mean ± SEM for each dose and ratio group tested per the legend and color map. Representative flow plots are shown in the right panel. **(B)** Percent OT-1 CD8+ T-cells in the peripheral blood for days 7 and 17 (before and after boost), plus expression of CD44 on endogenous CD8+ T-cells (middle panel). Graphs show mean ± SEM. Statistics analysis performed was Mann-Whitney, two-tailed, test. *p<0.05, **p<0.01, ***p<0.001, 'ns' p>0.05, not significant.

## Generation of Memory and Effector T-cell Populations

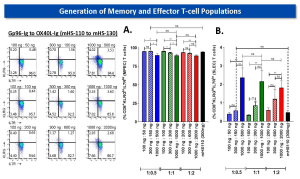


**Figure 4: Dose-dependent generation of MPEC+ and SLEC+ upon vaccination with mHS-110 and mHS-130**
Mice were tail bled consecutively on days post-immunization and boosts, and then stained for flow cytometry. Graph shows mean ± SEM for each dose and ratio group tested per the legend and color map. Representative flow plots are shown in the left panel. **(A)** Memory Precursor Effector Cells (MPEC); **(B)** Short Lived Effector Cells (SLEC) for endogenous CD8+ T-cell populations. Statistics analysis performed was Mann-Whitney, two-tailed, test. *p<0.05, **p<0.01, ***p<0.001, 'ns' p>0.05, not significant.

## Variable Ratio; Fixed Dose Vaccine Combination with Tumor Challenge

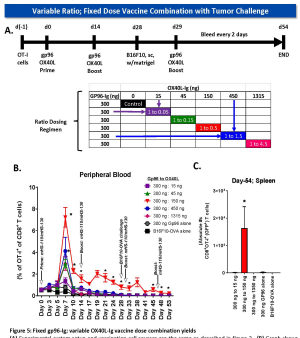


**Figure 5: Fixed gp96-Ig; variable OX40L-Ig vaccine dose combination yields**
**(A)** Experimental system setup and vaccination cell sources are the same as described in figure 2. **(B)** Graph shows mean ± SEM for each dose and ratio group tested per the legend and color map. **(C)** Absolute cell numbers for OT-1 CD8+ T-cells in the spleen for the final study day, 54. Graphs show mean ± SEM. Statistics analysis performed was Mann-Whitney, two-tailed, test. *p<0.05, **p<0.01, ***p<0.001, 'ns' p>0.05, not significant.

## Combination Vaccine Regimen and Response to Tumor Challenge

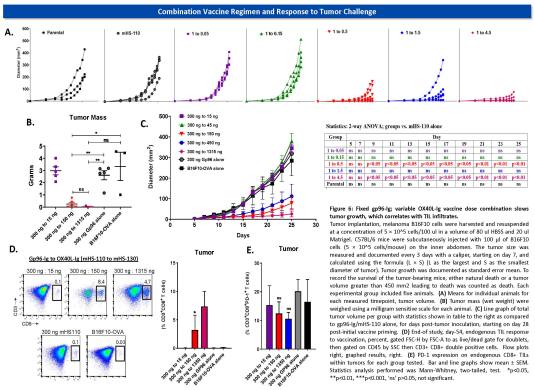


**Figure 6: Fixed gp96-Ig; variable OX40L-Ig vaccine dose combination slows tumor growth, which correlates with TIL infiltrates.**
Tumor implantation, melanoma B16F10 cells were harvested and resuspended at a concentration of 5 × 10^5 cells/100 ul in a volume of 80 ul HBSS and 20 ul Matrigel. C57BL/6 mice were subcutaneously injected with 100 µl of B16F10 cells (5 × 10^5 cells/mouse) on the inner abdomen. The tumor size was measured and documented every 3 days with a caliper, starting on day 7, and calculated using the formula (L × S) (L as the largest and S as the smallest diameter of tumor). Tumor growth was documented as standard error mean. To record the survival of the tumor-bearing mice, either natural death or a tumor volume greater than 450 mm2 leading to death was counted as death. Each experimental group included five animals. **(A)** Means for individual animals for each measured timepoint, tumor volume. **(B)** Tumor mass (wet weight) were weighed using a milligram sensitive scale for each animal. **(C)** Line graph of total tumor volume per group with statistics shown in table to the right as compared to gp96-Ig/mHS-130 alone, for days post-tumor inoculation, starting on day 28 post-initial vaccine priming. **(D)** End-of study, day-54, endogenous TIL response to vaccination, percent, gated FSC-H by FSC-A to as live/dead gate for doublets, then gated on CD45 by SSC then CD3+ CD8+ double positive cells. Flow plots right, graphed results, right. **(E)** PD-1 expression on endogenous CD8+ TILs within tumors for each group tested. Bar and line graphs show mean ± SEM. Statistics analysis performed was Mann-Whitney, two-tailed, test. *p<0.05, **p<0.01, ***p<0.001, 'ns' p>0.05, not significant.

## Conclusions

- Combination of an allogeneic tumor line expressing gp96-Ig and OX40L-Ig is a potent stimulator of anti-tumor CD8+ T-cell immune responses in animals
- Best ratio of gp96-Ig to OX40L-Ig falls within the range of 1-to-0.5 and 1-to-1; with 1-to-0.5 providing the best expansion and anti-tumor immunity
- Addition of OX40L-Ig secreting cells to gp96-Ig provides a synergistic impact on both transferred and endogenous tumor specific T-cells
- The minimal active biological dose for this combination is 100 ng of gp96-Ig to 50 ng of OX40L

## Acknowledgments & Contact Info

We would like to acknowledge the laboratories that have helped make these reagents and model systems possible: Drs. Natasa Strbo & Robert Levy from University of Miami and our previous lab director, Dr. Louis Gonzalez, for establishing the model system that made this data possible

*Corresponding Author: Matthew M. Seavey, Senior Director of Research, mseavey@heatbio.com

## References

1. Nicchitta CV, Nature Reviews Immunology. Opinion: Re-evaluating the role of heat-shock protein-peptide interactions in tumour immunity. Vol-3, May 2003
2. Strbo N, Garcia-Soto A, Schreiber TH, Podack ER. Secreted heat shock protein gp96-Ig: next-generation vaccines for cancer and infectious diseases. Immunologic research 2013;57:311-25.
3. Fromm G, de Silva S, Giffin L, Xu X, Rose J, Schreiber TH. Gp96-Ig/Costimulator (OX40L, ICOSL or 4-1BBL) Combination Vaccine Improves T-cell Priming and Enhances Immunity, Memory, and Tumor Elimination. Cancer Immunol Res. 2016 Sep 2;4(9):766-78.
4. Croft M, So T, Duan W, Soroosh P. The significance of OX40 and OX40L to T-cell biology and immune disease. Immunol Rev. 2009 May 229 (1): 173-91

**EXHIBIT 99.2**


**Heat Biologics Delivers Poster Presentation at the AACR Annual Meeting 2019**

*Animal study demonstrates combination of HS-110 and HS-130 yields three-fold increase in anti-tumor CD8+ T-cell expansion*

**DURHAM, NC – April 2, 2019** – Heat Biologics, Inc. (NASDAQ: HTBX), a biopharmaceutical company developing immunotherapies designed to activate a patient's immune system against cancer, announces that it delivered a poster presentation yesterday, April 1, 2019, at the American Association for Cancer Research (AACR) Annual Meeting. The Company's presentation, entitled, "Generation of a novel, allogeneic cell-based, Gp96-Ig/OX40L cancer vaccine, improves anti-tumor immunity and long-term memory T-cell generation," is available online here.

The poster presentation featured the Company's next generation cellular vaccine platform, *ComPACT* (COMbination Pan-Antigen Cytotoxic Therapy), which incorporates a tumor antigen chaperone (gp96-Ig) with T-cell costimulation (OX40L-Ig), simulating a single tumor cell line source that secretes both products. The presentation modeled how the addition of human HS-130, which secretes OX40L-Ig, to HS-110 may impact anti-tumor immune responses. This combination generated a three-fold increase in CD8+ T-cell expansion, increased numbers of long-lived tumor-specific T-cells, and potent short-lived killer T-cells required for tumor growth control.

Matt Seavey, Ph.D., Heat's Senior Director of Research, commented, "We are highly encouraged by these preliminary results in a mouse model, which demonstrate that the combination of HS-110 with OX40L co-stimulation has the potential to dramatically enhance anti-tumor immune responses. Moreover, this study further informed our selection of the ideal ratio of gp96 to OX40L, which will be helpful as we prepare to file an IND for our HS-130 *ComPACT* trial later this quarter."

**About AACR Annual Meeting 2019**

The AACR Annual Meeting program covers the latest discoveries across the spectrum of cancer research—from population science and prevention; to cancer biology, translational, and clinical studies; to survivorship and advocacy—and highlights the work of the best minds in research and medicine from institutions all over the world.

**About Heat Biologics, Inc.**

Heat Biologics is a biopharmaceutical company developing immunotherapies designed to activate a patient's immune system against cancer using of CD8+ "Killer" T-cells. Our T-Cell Activation Platform ("TCAP") produces therapies designed to turn "cold" tumors "hot" and be administered in combination with checkpoint therapies and other immuno-modulators to increase their effectiveness. HS-110 is our first biologic product candidate in a series of proprietary immunotherapies designed to stimulate a patient's own T-cells to attack cancer. Our *ComPACT* technology is the first potential, dual-acting immunotherapy designed to deliver T-cell activation and co-stimulation in a single product. We are currently enrolling patients in our Phase 2 clinical trial for advanced non-small cell lung cancer, in combination with Bristol-Myers Squibb's nivolumab (Opdivo®) and with Merck's pembrolizumab (Keytruda®). Pelican Therapeutics, a subsidiary of Heat, is focused on the development of co-stimulatory monoclonal antibody and fusion protein-based therapies designed to activate the immune system. For more information, please visit www.heatbio.com.

**Forward Looking Statements**

*This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 on our current expectations and projections about future events. In some cases, forward-looking statements can be identified by terminology such as "may," "should," "potential," "continue," "expects," "anticipates," "intends," "plans," "believes," "estimates," and similar expressions. These statements are based upon current beliefs, expectation, and assumptions and include statements that the addition of human HS-130, which secretes OX40L-Ig, to HS-110 may impact anti-tumor immune responses and that the combination of HS-110 with OX40L co-stimulation has the potential to dramatically enhance anti-tumor immune responses. These statements are subject to a number of risks and uncertainties, many of which are difficult to predict, including the ability of Heat's therapies to perform as designed, to demonstrate safety and efficacy, as well as results that are consistent with prior results,* including clinical results of the combination of the combination of HS-110 with OX40L co-stimulation that are consistent with the results presented in the poster*, the ability to enroll patients and complete the clinical trials on time and achieve desired results and benefits, Heat's ability to obtain regulatory approvals for commercialization of product candidates or to comply with ongoing regulatory requirements, regulatory limitations relating to Heat's ability to promote or commercialize its product candidates for specific indications, acceptance of its product candidates in the marketplace and the successful development, marketing or sale of products, Heat's ability to maintain its license agreements, the continued maintenance and growth of its patent estate, its ability to establish and maintain collaborations, its ability to obtain or maintain the capital or grants necessary to fund its research and development activities, and its ability to retain its key scientists or management personnel, and the other factors described in Heat's Annual Report on Form 10-K for the year ended December 31, 2018 and Heat's other filings with the SEC. The information in this release is provided only as of the date of this release, and Heat undertakes no obligation to update any forward-looking statements contained in this release based on new information, future events, or otherwise, except as required by law.*

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