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Heat Biologics Presents Interim Phase 2 Lung Cancer Data on HS-110 + Nivolumab at ASCO-SITC Clinical Immuno-Oncology Symposium

- Preliminary data suggests the addition of HS-110 to Nivolumab may restore responsiveness to treatment after tumor progression on prior checkpoint inhibitor therapy

- Median overall survival not yet reached with median follow up of 14.4 months in Cohort A

- Improved survival observed in patients with low CD8+ "cold" tumor at baseline compared to high CD8+ patients

- Occurrence of injection site reactions correlates with improved overall survival

SAN FRANCISCO, CA / ACCESSWIRE / February 28, 2019 /Heat Biologics, Inc. (NASDAQ: HTBX), a biopharmaceutical company developing immunotherapies designed to activate a patient's immune system against cancer, today announced updated interim results from its ongoing Phase 2 study investigating HS-110 in combination with Bristol-Myers Squibb's anti-PD-1 checkpoint inhibitor, nivolumab (Opdivo®), in patients with advanced non-small cell lung cancer (NSCLC). The results were presented today at the ASCO-SITC Clinical Immuno-Oncology Symposium by Daniel Morgensztern, M.D., Associate Professor of Medicine and Director of Thoracic Oncology, Washington University School of Medicine, and Lead Investigator in the trial. Data were presented on both Cohort A and Cohort B of the trial. Cohort A enrolls only previously treated patients who have never received a checkpoint inhibitor (CPI), while Cohort B enrolls patients who received a minimum of 4 months of treatment with a CPI as part of their prior therapy, but subsequently had documented progressive disease.

"The treatment landscape for NSCLC has fundamentally changed as the number of patients who receive first line checkpoint inhibitor therapy is rapidly increasing," said COL(ret) George E Peoples, MD, FACS, Heat's Chief Medical Advisor. "The preliminary data from our Cohort B is increasingly relevant and potentially exciting as it suggests that the addition of HS-110 to nivolumab may restore anti-tumor activity in patients whose disease has progressed after treatment with a CPI."

Jeff Hutchins, Ph.D., Chief Scientific and Operating Officer of Heat said, "The observed response rates and durability of disease stabilization support our mechanistic hypothesis

that the broad, T-cell mediated immune response activated by HS-110 may improve patient survival when administered in combination with a CPI. The Cohort B data suggest that HS-110 may improve clinical outcomes for patients who have lost the benefit of treatment with a checkpoint inhibitor. We look forward to completing enrollment in this trial in Q2 and releasing additional results later this year as the data matures."

Highlights for both cohorts are presented below:

Cohort B (patients who progressed after ≥ 4 months of prior treatment with a checkpoint inhibitor)

- Of first 20 patients enrolled in this cohort:
  - Partial response (PR) in 3 patients (15%) per RECIST 1.1 and 4 patients (20%) per investigator assessment
  - Disease control rate (DCR) of 55%
- The 3 RECIST 1.1 PR patients had documented progression on CPI monotherapy immediately preceding study entry
- Median progression free survival (mPFS) was 2.7 months (95% CI; 1.8 - 4.0 months)

Cohort A (patients who have never received a CPI prior to study entry)

- Of 42 patients enrolled by the cutoff date:
  - PR in 9 patients (21%) per RECIST 1.1
  - DCR of 50%
  - Median overall survival not yet reached (60% still alive with a median follow-up of 14.4 months)
- Responses and disease stabilization are durable and long-lasting
- Subgroup analyses, predefined in the clinical protocol, were performed for levels of tumor-infiltrating lymphocytes (CD8+ TILs) present in tumors at baseline. A survival benefit [hazard ratio (HR) = 0.39] was observed in patients with levels CD8+ TIL $\leq$10% (i.e. "cold" tumors), a population that typically responds poorly to checkpoint inhibitors. The treatment benefit appeared to be independent of PD-L1 status (HR = 0.85)
- Immune reactivity to HS-110 was measured via ELISPOT assay (high vs. low compared to median) on patient peripheral blood mononuclear cells obtained before and during treatment with a median overall survival benefit of 6.2 months in the high ELISPOT group
- Overall survival was significantly higher in patients that experienced at least one dermal injection site reaction to HS-110 at any time during study treatment, supporting HS-110's mechanism of action (HR = 0.15 [95% CI: 0.05-0.45], p=0.0001)

For both cohorts, treatment with HS-110 in combination with nivolumab was well tolerated, with no additional toxicities beyond those observed with single agent CPI therapy.

Importantly, data from Cohort B suggest that HS-110 in combination with nivolumab reduced tumor burden in patients whose disease progressed after treatment with a checkpoint inhibitor at any time prior to study entry. Additionally, the deepest responses

were observed in three patients whose last treatment immediately preceding enrollment was checkpoint inhibitor monotherapy.

Also of interest is the data regarding overall survival (OS) in patients with low CD8+ TIL (tumor infiltrating lymphocytes) at baseline. Protocol-defined subgroup analysis of patients categorized as 'high' or low' TIL, based on levels of CD8+ cells present in the stroma of their tumor tissue at baseline, demonstrate a survival advantage for the 'low TIL' group as compared to the 'high TIL' group (not reached vs. 13.8 months; HR = 0.39 [95% CI; 0.06-2.31]. These data are very encouraging as prior studies with nivolumab alone suggest that "cold" tumor patients with lower levels of baseline CD8+ TILs have lower response rates compared to "hot" tumor patients with high levels of CD8+ TILs.

Trial results are summarized in the company'supdated corporate presentation, along with the official ASCO-SITC poster.

Trial Design

The Phase 2 trial is designed to evaluate the safety and efficacy of HS-110 combined with an immune checkpoint inhibitor for the treatment of advanced non-small cell lung cancer. Patients receive weekly HS-110 (1 x 107 cells) administered as 5 intradermal 0.1 mL injections for 18 weeks in combination with bi-weekly nivolumab 240 mg IV administered until confirmed disease progression or unacceptable toxicity, whichever occurs first. The primary endpoint is objective response rate (ORR); secondary endpoints include overall survival (OS), progression-free survival (PFS), disease control rate (DCR) and duration of response (DOR). Exploratory endpoints include correlation of clinical outcomes to baseline CD8+ TILs, PD-L1 expression, peripheral blood tumor mutation burden and ELISPOT analysis.

For further details about the trial and the results presented at ASCO-SITC, refer to Heat Bio's updated corporate presentation, which can be found on the Investors tab of the corporate website https://ir.heatbio.com/.

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 regarding the suggestion that the addition of HS-110 to Nivolumab may restore responsiveness to treatment after tumor progression on prior checkpoint inhibitor and the suggestion that HS-110 may improve clinical outcomes for patients who have lost the benefit of treatment with a checkpoint inhibitor. 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, 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 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.

[1]S Sahba A-L. Niemeijer J. De Langen E. Thunnissen, Annals of Oncology, Volume 28, Issue suppl 5, September 1, 2017

Media and Investor Relations Contact

David Waldman
+1 919 289 4017
investorrelations@heatbio.com

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