HOOKIPA Pharma Presents Additional Preliminary Phase 2 Data on HB-200 in Combination with Pembrolizumab as First-Line Treatment in Patients with HPV16+ Head and Neck Cancers at European Society for Medical Oncology Congress 2023

October 22, 2023 at 6:01 AM EDT

- *42 percent objective response rate (ORR) was observed among 19 evaluable patients with recurrent/metastatic head and neck cancer in the first-line setting —doubling historical ORR reported with pembrolizumab alone[1]*
- *Strong immunogenicity and activation of antigen-specific CD8+ T cells observed*
- *Data reinforce HOOKIPA's commitment to start a randomized trial of HB-200 in combination with pembrolizumab as 1st-line treatment of recurrent/metastatic HPV16+ head and neck cancer in 2024*
- *Data presented at the European Society for Medical Oncology Congress 2023*

NEW YORK and VIENNA, Austria, Oct. 22, 2023 (GLOBE NEWSWIRE) -- HOOKIPA Pharma Inc. (NASDAQ: HOOK, 'HOOKIPA'), a company developing a new class of immunotherapeutics based on its proprietary arenavirus platform, today presented updated data from its ongoing Phase 2 trial of HB-200 in combination with pembrolizumab in patients with recurrent/metastatic Human Papillomavirus 16-positive (HPV16+) head and neck cancer.

The preliminary data presented at the European Society for Medical Oncology (ESMO) Congress 2023 showed a 42 percent confirmed objective response rate (ORR) and disease control rate (DCR) of 74 percent across 19 evaluable patients treated with HB-200 in combination with pembrolizumab in the 1st-line, checkpoint inhibitor (CPI)-naïve setting, doubling the 19 percent ORR for pembrolizumab alone[1]. Best overall response for the evaluable population included one patient with a confirmed complete response, seven patients with confirmed partial responses, and six patients with stable disease. All evaluable patients were alive at the data cutoff (DCO), and the median follow-up time at DCO was 8.3 months. Median overall survival and progression-free survival data are still maturing.

Importantly, results showed significant activation of antigen-specific CD8+ T cells, the body's primary driver of tumor killing activity. Out of 17 patients with available peripheral blood mononuclear cells (PMBC) samples, all patients showed an increase of tumor antigen-specific circulating HPV16+ CD8+ T cells. These T cell activation data are consistent with previously reported monotherapy data for HB-200.

"We have observed objective response rate, disease control rate, and activation of antigen-specific T cells which demonstrate the potential of the intended mechanism to stimulate the immune system to combat tumors. We have also observed generally favorable tolerability to date among the patient population, supporting the investigational therapy's potential in combination settings," said Dr. Alan L. Ho, Head and Neck Oncologist at Memorial Sloan Kettering Cancer Center and a trial investigator.

"We continue to see encouraging results in the first-line patient setting for our HB-200 trial in combination with pembrolizumab as we have consistently observed patient responses that are double the ORR observed in standard of care treatments alone—reinforcing previously reported data," said Joern Aldag, Chief Executive Officer at HOOKIPA. "These results give us great conviction to proceed with our planned randomized trial."

Results:
HB-200 in combination with pembrolizumab in the 1st-line setting (NCT04180215)
As of the DCO, August 7, 2023, the updated interim efficacy analysis included 19 evaluable patients with at least two imaging assessments out of the first 20 patients with HPV16+ recurrent/metastatic head and neck cancers treated with HB-200 in combination with pembrolizumab in the 1st-line setting as part of the Phase 2 trial. Of the intent-to-treat population (n=20) one patient was not evaluable due to COVID-related death prior to the first tumor scan. All patients received HB-200 intravenously every three weeks for the first five doses and every six weeks thereafter. HB-200 is a 2-vector investigational therapy with alternating administration of Lymphocytic Choriomeningitis Virus (LCMV), and Pichinde Virus (PICV) vectors, encoding the same HPV16 E6/E7 antigens.

HB-200 in combination with pembrolizumab demonstrated promising initial anti-tumor activity with a 42 percent ORR (8 of 19 evaluable patients with confirmed responses by investigator assessment under RECIST 1.1) among CPI-naïve patients with 1st-line recurrent/metastatic HPV16+ PD-L1+ head and neck cancer. These data represent a doubling of the 19 percent ORR reported for pembrolizumab alone[1] and are consistent with previously reported HB-200 data. Eight patients responded including one with a confirmed complete response and seven with confirmed partial responses. Another six patients achieved stable disease representing a DCR of 74 percent (14 of 19 patients). While recruitment is ongoing, based on these data, HOOKIPA is preparing to start a randomized trial of HB-200 in combination with pembrolizumab as 1st-line treatment of recurrent/metastatic HPV16+ PD-L1+ head and neck cancers in 2024.

Immunogenicity
Tumor-specific CD8+ T cell levels induced by HB-200 in combination with pembrolizumab are unprecedented and consistent with levels observed with HB-200 monotherapy. Among the 17 patients with available peripheral blood mononuclear cells (PMBC) samples, all patients showed an increase in the percent of tumor antigen-specific circulating HPV16+ CD8+ T cell responses per intercellular cytokine staining analysis. Peak percentage of antigen-specific circulating HPV16+ CD8+ T cell responses reached up to 31 percent with a median of 3.36 percent. Max response on treatment vs. before treatment of systemic HPV-16 E7 and E6 specific T cells measured by ELISPOT showed that the median fold-increase for these patients' total

tumor specific T cells was a 451-fold increase over baseline, with the maximal increase of 4,000-fold.

Safety and tolerability profile
Results from the HB-200 in combination with pembrolizumab in 1st-line patients arm of the Phase 2 part of the trial showed that HB-200 was generally well tolerated among 20 patients treated. Two patients (10 percent) showed serious adverse events related to the treatment with HB-200 or pembrolizumab. Only one patient (5 percent) discontinued due to a treatment-related adverse event (related to pembrolizumab). The updated safety profile adds to the previously reported safety and tolerability data from all 132 patients across all arms of the trial who received HB-200 monotherapy or HB-200 in combination with pembrolizumab. This generally favorable tolerability profile highlights the potential of HB-200—and arenaviral immunotherapies in general—to be successfully combined with other immunotherapies where tumor antigen-specific T cell induction is of potential benefit.

ESMO HB-200 Poster Presentation

Title: HB-200 Arenavirus-Based Immunotherapy Plus Pembrolizumab as a First-Line Treatment in Patients with Recurrent/Metastatic HPV16-Positive Head and Neck Cancer
Presenter: Dr. Alan L. Ho, Head and Neck Oncologist at Memorial Sloan Kettering Cancer Center and a trial investigator
Session Date: October 22, 2023
Poster Board Number: 921P
Abstract Number: 2212

About HB-200
HB-200 is HOOKIPA's lead oncology candidate engineered with the company's proprietary replicating arenaviral vector platform. HB-200 is an alternating 2-vector immunotherapy designed to focus the immune response against the encoded antigen. It comprises two single-vector compounds with arenaviral backbones based on LCMV and PICV. Both encode and express an identical E7E6 fusion protein, comprising well characterized tumor-specific antigens for HPV16+ cancers. HB-200 in combination with pembrolizumab received Fast Track Designation from the U.S. Food and Drug Administration for the treatment of 1st-line recurrent/metastatic HPV16+ head and neck cancers.

About the HB-200 trial (NCT04180215)
This Phase 1/2 clinical trial is an open-label trial evaluating HB-200 for the treatment of advanced HPV16+ cancers. Phase 1 assessed various dose levels, regimen, and modes of administration in a post-standard of care setting. Based on safety and tolerability, initial anti-tumor activity and T cell response data, HB-200 was advanced for further development in Phase 2. The Phase 2 part of the trial is open label with primary endpoints of efficacy based on objective response and disease control rate as defined by RECIST 1.1 and iRECIST. The trial is evaluating HB-200 in combination with pembrolizumab in the 1st-line and 2nd-line plus settings, as well as HB-200 alone in the post-standard of care setting.

About Human Papillomavirus-driven Cancers
Human Papillomavirus, or HPV, is a common viral infection estimated to cause about 5 percent of the worldwide cancer burden. This includes up to 60 percent of head and neck, 89 percent of cervical, 78 percent of vaginal, 88 percent of anal, 67 percent of vulvar and 50 percent of penile cancers.

While there are numerous HPV types associated with cancer, HPV16 is the most common cause of cancer. Most HPV infections are cleared from the body with no lasting consequences. However, in some cases, HPV DNA becomes integrated into chromosomal DNA. When host cells take up this DNA, they express the HPV E6 and E7 proteins. This uptake can potentially lead to cancer since expression of these proteins leads to alterations in cell cycle control, which in turn predisposes these cells to become cancerous.

About HOOKIPA
HOOKIPA Pharma Inc. (NASDAQ: HOOK) is a clinical-stage biopharmaceutical company focused on developing novel immunotherapies, based on its proprietary arenavirus platform, which are designed to mobilize and amplify targeted T cells and thereby fight or prevent serious disease. HOOKIPA's replicating and non-replicating technologies are engineered to induce robust and durable antigen-specific CD8+ T cell responses and pathogen-neutralizing antibodies. HOOKIPA's pipeline includes its wholly owned investigational arenaviral immunotherapies targeting Human Papillomavirus 16-positive cancers, prostate cancers, and other undisclosed programs. HOOKIPA is collaborating with Roche on an arenaviral immunotherapeutic for KRAS-mutated cancers. In addition, HOOKIPA aims to develop functional cures of HBV and HIV in collaboration with Gilead.

Find out more about HOOKIPA online at www.hookipapharma.com.

[1] Harrington et al. Pembrolizumab With or Without Chemotherapy in Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma: Updated Results of the Phase III KEYNOTE-048 Study. *Journal of Clinical Oncology.* 2023;41(4);790-802.

Forward Looking Statements
Certain statements set forth in this press release constitute "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements can be identified by terms such as "believes," "expects," "plans," "potential," "would" or similar expressions and the negative of those terms. Such forward-looking statements involve substantial risks and uncertainties that could cause HOOKIPA's research and clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in the drug development process, including HOOKIPA's programs' early stage of development, the process of designing and conducting preclinical and clinical trials, the risk that interim or preliminary data may differ from final data from clinical trials, the regulatory approval processes, the timing of regulatory filings, the challenges associated with manufacturing drug products, HOOKIPA's ability to successfully establish, protect and defend its intellectual property, risks relating to business interruptions resulting from public health crises, the impact of public health crises on the enrollment of patients and timing of clinical results, and other matters that could affect the sufficiency of existing cash to fund operations. HOOKIPA undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the company in general, see HOOKIPA's quarterly report on Form 10-Q for the quarter ended June 30, 2023, which is available on the SEC's website at www.sec.gov and HOOKIPA's website at www.hookipapharma.com.

Investors and others should note that we announce material financial information to our investors using our investor relations website (https://ir.hookipapharma.com/), SEC filings, press releases, public conference calls and webcasts. We use these channels, as well as social media, to communicate with our members and the public about our company, our services and other issues. It is possible that the information we post on social

media could be deemed to be material information. Therefore, we encourage investors, the media, and others interested in our company to review the information we post on the U.S. social media channels listed on our investor relations website.

For further information, please contact:

Media
Instinctif Partners
hookipa@instinctif.com
+44 (0) 7457 2020

Investors
Michael Kaiser, Investor Relations
michael.kaiser@hookipapharma.com
+1 (917) 984-7537