HOOKIPA Phase 1 HB-200 data show unprecedented T cell response, favorable tolerability, and preliminary efficacy as monotherapy for advanced HPV16+ cancers

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- Novel arenaviral therapeutic HB-200 generates outstanding tumor antigen-specific CD8+ T cell responses (average of 6 percent and up to 40 percent of T cell pool)
- To-date, HB-201 monotherapy has shown 18 percent overall response rate and median progression-free survival of 3.45 months in heavily pretreated head and neck cancer patients
- Clinical data replicate pre-clinical results, showcasing the potential of HOOKIPA's arenaviral platform to produce multiple potent cancer immunotherapies

NEW YORK and VIENNA, Austria, June 07, 2021 (GLOBE NEWSWIRE) -- HOOKIPA Pharma Inc. (NASDAQ: HOOK, 'HOOKIPA'), a company developing a new class of immunotherapeutics based on its proprietary arenavirus platform, today reported positive Phase 1 data from its ongoing Phase 1/2 study (NCT04180215) of HB-200 for the treatment of advanced Human Papillomavirus 16-positive (HPV16+) cancers. Data presented as an oral presentation (abstract #2502) at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting showed outstanding T cell responses, preliminary efficacy as a monotherapy in heavily pretreated patients who progressed on standard of care, including checkpoint inhibitors, and favorable tolerability. The company also announced translational data suggesting a relationship between T cell response and potential clinical efficacy. The company will host an investor event today at 6:30pm EDT.

"Our early Phase 1 HB-200 data provide compelling clinical evidence of the potential of our versatile arenaviral platform to introduce a new class of immunotherapeutics that can generate an unprecedented T cell response to the desired cancer target," said Joern Aldag, Chief Executive Officer at HOOKIPA. "We're in dose escalation phase in a group of heavily pre-treated HPV16+ cancer patients, so we're thrilled to see response rates with HB-201 monotherapy in head and neck cancer patients that one would expect only in earlier lines of therapy. Moreover, initial clinical biopsy data validate the proof of mechanism, highlighting the potential for our technology to address unmet needs across various cancers. We're excited to share further data as the HPV16+ cancer trial continues, and we look forward to initiating registration-enabling studies in early 2022."

Up to the March 31 cut-off date, 38 patients with metastatic HPV16+ tumors had received HB-200 therapy: 14 received HB-201 intravenously every three weeks, 8 received alternating HB-201/HB-202 intravenously every three weeks, and 16 received other regimens. Most of the patients (32) have squamous cell head and neck tumors; patients with other tumor types included three with cervical, one with vaginal, one with anal, and one with penile. Participants received a median of three prior therapies (ranging from one to 10), and 82 percent (31 participants) had progressed on a checkpoint inhibitor regimen. Seventy-nine percent had baseline distant metastasis, underscoring the difficult-to-treat patient population.

Immunogenicity results

Preliminary data show that HB-200 therapy is highly immunogenic, inducing unprecedented levels of activated, tumor antigen-specific CD8+ T cells. Immunogenicity data for eight patients with head and neck tumors were available at the time of data cut-off: six received HB-201 dose level 2 and two received alternating HB-201/HB-202 dose level 1. CD8+ T cell immunogenicity was assessed using direct Enzyme-Linked ImmunoSpot (ELISpot) T cell analysis and intracellular cytokine staining (ICS) followed by flow cytometry. ELISpot is used to quantify antigen-specific T cells in the blood whereas flow cytometry differentiates antigen-specific CD8+ T cells (killer T cells) from antigen-specific CD4+ T cells (helper cells). CD8+ T cells play a critical role in fighting cancer and infections.

At baseline, all patients had nearly undetectable levels of tumor-specific T cells. Within two weeks of a single dose of HB-200, all patients showed increased tumor-specific CD8+ T cell levels; all responses well exceeded the lower limit of quantification, and many approached the upper limit of quantification. Importantly, these results are based on direct ELISpot without *ex vivo* expansion of T cells, highlighting the magnitude of T cell response generated by HB-200 therapy. (*Ex vivo* expansion is often used to amplify responses otherwise not measurable).

Furthermore, flow cytometric analysis showed HB-200 therapy induced outstanding tumor-specific CD8+ T cell responses, including an average of 6 percent and up to 40 percent of the circulating T cell pool. (Of note, the latter was observed after alternating HB-201/HB-202 administration.) While there is no established threshold, a level of mid-single digit percentage, such as 5 percent, is a strong indicator of response. Both findings are consistent with pre-clinical observations, highlighting the potential of HOOKIPA's proprietary arenaviral platform to deliver a new class of immunotherapeutics. The data are from the ongoing Phase 1 dose escalation; the recommended Phase 2 dose for HB-200 therapy has yet not been reached.

Translational results

Early translational data collected to-date suggest a relationship between T cells and clinical efficacy. Specifically, response rates and progression-free survival improve with higher dose levels and also with alternating, 2-vector therapy. In addition, paired biopsy data showed that HB-200 therapy induced similar increases in CD8+ T cells in both blood and tumor tissue. There is early evidence from tissue samples that HB-200 decreases immune suppression in the tumor microenvironment.

Preliminary efficacy results

As of the data cut-off, 15 patients with metastatic head and neck cancers were eligible for the efficacy analysis: 11 received HB-201 intravenously every three weeks and four received HB-201/HB-202 intravenously every three weeks. While treatment continues for these patients, the Phase 1 data

show promising treatment duration with a median of 127 days for HB-201 recipients and 87 days for HB-201/HB-202 recipients at data cut-off. HB-201 dose level 2 may lead to prolonged treatment compared to dose level 1, whereas both dose levels of HB-201/HB-202 are ongoing.

Of the 15 patients, 93 percent (14/15 patients) had target lesion control, including 53 percent (8/15 patients) with target lesion reduction. Two of the 14 patients progressed at other sites, resulting in an overall disease control rate of 80 percent (12/15 patients). In particular, HB-201 monotherapy demonstrated an 18 percent overall response rate and an ongoing 3.45-month median progression-free survival (PFS). These results are particularly notable given the heavily pre-treated population (median of 3 prior treatments) and the historical lack of clinical response of active immunization therapies as monotherapies. In addition, HB-201 showed a 73 percent (8/11 patients) disease control rate, with two partial responses and six patients with stable disease, including four with stable disease for more than 16 weeks. Preliminary data on HB-201/HB-202 showed a disease control rate of 100 percent (4/4 patients).

Safety results

The Phase 1 data on 38 evaluable patients show that HB-200 therapy has a favorable safety profile in heavily pre-treated patients with HPV16+ cancers, underlining its potential as a monotherapy and in possible combination with checkpoint inhibitors. Treatment-related adverse events were reported in 53 percent of patients. There were no serious adverse events, no dose-limiting toxicities and no treatment-related adverse events rated grade 3 or higher. In addition, there were no discontinuations, dose changes or interruptions resulting from treatment-related adverse events. The most common side effects were fatigue (32 percent), fever (26 percent), nausea (18 percent) and hypertension (16 percent).

“Treatment options for patients with advanced HPV16+ cancers are limited, and there is no established standard of care following checkpoint inhibitor use,” said Alan L. Ho, M.D., Ph.D., a medical oncologist at Memorial Sloan Kettering Cancer Center and a trial investigator. “Response rates are expected to decline with subsequent lines of therapy, so it’s encouraging to see an active immunization therapy, like HB-201 monotherapy, result in objective responses in heavily pre-treated patients. In addition, the unprecedented levels of antigen-specific CD8+ T cells induced by HB-201/HB-202 are promising and support the potential to convert immunogenicity into clinical efficacy.”

Investor Event

HOOKIPA will host a live webcast event, “Advancing novel immunotherapies: HOOKIPA ASCO data review,” today at 6:30 p.m. EDT. Joern Aldag, Chief Executive Officer, and Igor Matushansky, M.D., Ph.D., Chief Medical Officer, will provide an overview of the ASCO oral data and future plans for HOOKIPA’s oncology program. Dmitriy Zamarin, M.D., Ph.D., Translational Research Director in Gynecologic Medical Oncology at Memorial Sloan Kettering Cancer Center and a co-investigator in this study, will also offer commentary on the significance and implications of the translational findings. This event will be broadcast via Zoom Webinar and you may participate in the Q&A from Zoom.

To participate by phone, dial +1 (929) 205 6099 (US) or +44 330 088 5830 (International), webinar ID: 882 5139 3861# and press *9 when prompted to ask a question. The webcast and the presentation will be available within the Investors & Media section of HOOKIPA’s website at https://ir.hookipapharma.com/events. A recording of the event will be available for 30 days.

About HB-201/HB-202

HB-201 and HB-202 are HOOKIPA’s lead oncology candidates engineered with the company’s proprietary replicating arenaviral vector platform. Each single-vector compound uses a different arenavirus backbone (Lymphocytic Choriomeningitis Virus for HB-201 and Pichinde Virus for HB-202), while expressing the same antigen, an E7E6 fusion protein derived from HPV16. In pre-clinical studies, alternating administration of HB-201 and HB-202 we observed in a ten-fold increase in immune response and better disease control than either compound alone.

About the trial (NCT04180215)

This Phase 1/2 clinical trial is an open-label trial exploring different dose levels and dosing schedules in individuals with treatment-refractory HPV16+ cancers who progressed on standard of care, including check point inhibitors. The primary endpoint of the Phase 1 is a recommended Phase 2 dose. Secondary endpoints include safety and tolerability, as well as preliminary efficacy defined by RECIST 1.1. The study also includes exploratory objectives on immunogenicity and pharmacodynamic biomarkers.

The trial is evaluating HB-201 as a monotherapy, as an alternating 2-vector therapy with HB-202, and in combination with a PD-1 inhibitor. Participants receive HB-201/HB-202 intravenously or, for patients with an accessible lesion, the first dose can be delivered via intratumoral injection followed by intravenous dosing. Dosing every three weeks and every two weeks is being explored, as well as different dose levels. Enrollment is ongoing and HOOKIPA expects to share additional clinical, translational and biomarker data at upcoming medical conferences.

About Human Papillomavirus

Human Papillomavirus, or HPV, is estimated to cause about 5 percent of the worldwide burden of cancers. This includes approximately 99 percent of cases in cervical, up to 60 percent of head and neck, 70 percent of vaginal and 88 percent of anal cancers.

The majority of these cancers are caused by the HPV serotype 16. Most infections with HPV 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 that mobilize and amplify targeted T cells and antibodies, the body’s natural infection killers, to fight or prevent serious disease.

HOOKIPA is developing a broad pipeline of potential first-in-class arenaviral immunotherapies in oncology and infectious disease. We are leveraging our proprietary, versatile platform to engineer arenaviral therapeutics that induce robust antigen-specific CD8+ T cells and pathogen-neutralizing antibodies to a broad range of self and non-self antigens, including viral antigens, tumor-associated antigens and neoantigens. Our immunotherapies are designed to use either non-replicating or replicating viral vectors based on the target disease, with the potential to induce CD8+ T cell response levels previously not achieved by other immunotherapy approaches.

HOOKIPA’s pipeline include three ongoing clinical trials in Human Papilloma Virus 16-positive cancers and Cytomegalovirus, as well as preclinical research in prostate cancer, HIV and Hepatitis B. The latter two are in collaboration with Gilead Sciences, Inc.

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

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 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 the coronavirus (COVID-19) disease outbreak or similar public health crises, the impact of COVID-19 on the enrollment of patients and timing of clinical results for HB-101 and other programs, and other matters that could affect the sufficiency of existing cash to fund operations and HOOKIPA’s ability to achieve the milestones under the agreement with Gilead. 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 annual report on Form 10-Q for the financial year ended March 31, 2021 which is available on the Security and Exchange Commission’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.

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