HOOKIPA announces positive preliminary Phase 1 immunogenicity data for its immunotherapy candidates to treat advanced HPV16+ cancers

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- Preliminary data demonstrate a robust increase in HPV16+-specific T cells, including up to 8% of circulating CD8+ T cells, after one dose of HB-201 or HB-202
- Early data on HB-201 monotherapy show an increase in interferon-gamma and other immune stimulatory cytokines after a single dose, highlighting immune system activation
- Late-breaker data at AACR Annual Meeting reinforce promising anti-tumor activity reported in 2020 and underscore the potential of HOOKIPA's novel arenavirus platform to deliver transformational cancer therapies

NEW YORK and VIENNA, Austria, April 10, 2021 (GLOBE NEWSWIRE) -- HOOKIPA Pharma Inc. (NASDAQ: HOOK, 'HOOKIPA'), a company developing a new class of immunotherapeutics based on its proprietary arenavirus platform, today announced positive preliminary Phase 1 immunogenicity data for its lead oncology candidates, HB-201 and HB-202, to treat Human Papillomavirus 16-positive (HPV16+) cancers. The results are from an ongoing Phase 1/2 study (NCT04180215) currently investigating HB-201 as a single-vector therapy and HB-201 and HB-202 as an alternating two-vector therapy for the treatment of advanced metastatic HPV16+ cancers. The data were presented today at a late-breaker poster session at the virtual American Association for Cancer Research Annual Meeting.

"We're excited to see the quantity and quality of a targeted immune response, particularly the directly measured increase in HPV16+-specific CD8+ T cells, generated by a single dose of our lead oncology candidates, HB-201 or HB-202. As we are still exploring optimal dosing, these early responses are particularly encouraging," said Joern Aldag, Chief Executive Officer of HOOKIPA. "We believe our novel arenavirus platform has the potential to introduce a new class of immunotherapeutics that could considerably advance how physicians care for people with HPV16+ cancers. Building on the early clinical results reported on HB-201 in December, we look forward to additional data read-outs from our first clinical oncology program in the coming months."

Preliminary data showed a strong antigen-specific T cell response after one dose of HB-201 or HB-202, based on direct Enzyme-Linked ImmunoSpot (ELISpot) T cell analysis. (ELISpot is used to quantify antigen-specific T cells in the blood.) All 5 patients who received a single dose of HB-201 or HB-202 had a strong induction of T cells specific to HPV16+ cancer 2 weeks after administration. An up to 250-fold increase in antigen-specific T cells was observed 2 weeks after a single dose of HB-201 in 4 patients. One patient who received a single dose of HB-202 showed a 150-fold increase in antigen-specific T cells 2 weeks after administration. Importantly, the results are based on direct ELISpot without *ex vivo* expansion of T cells, underscoring the magnitude of T cell response generated by one dose of HB-201 or HB-202. (*Ex vivo* expansion is often used to amplify responses so that they are more easily measured.) The data are derived from dose level 2 of ongoing dose escalation, and the recommended Phase 2 doses for HB-201 and HB-202 have not been reached.

In addition, analysis of the antigen-specific T cell response showed an increase in CD8+ T cells specific to HPV16+ cancer after a single dose of HB-201 (baseline 0% to 2.8% two weeks later) and HB-202 (baseline 0% to 8.1% two weeks later). These data were assessed using intracellular cytokine staining (ICS) followed by flow cytometry, which differentiates antigen-specific CD8+ T cells (cytotoxic/killer T cells) from antigen-specific CD4+ T cells (helper T cells). Of note, the HPV16+ cancer patients included in this analysis had negligible levels of antigen-specific CD8+ T cells prior to treatment with HB-201 or HB-202.

Other preliminary immunogenicity data highlight immune system activation following a single dose of HB-201. Blood samples from 12 patients were assessed across 13 timepoints for levels of 30 different cytokines and chemokines, which play critical roles in activating an immune response. At the time of data cut-off, baseline and day 4 samples were available for 9 of the 12 patients. The analysis showed that, 4 days after a single dose of HB-201, interferon-gamma levels increased in 90% of patients, and an increase in other immune stimulatory cytokines and chemokines was observed. These data comprise an early sign of natural killer (NK) cell and/or T cell activation by HB-201.

"Treatment options are limited for people with metastatic HPV16+ cancers, and the likelihood for long-term survival is low," said Dmitriy Zamarin, MD, PhD, Translational Research Director in Gynecologic Medical Oncology at Memorial Sloan Kettering Cancer Center and co-investigator in this study. "We don't often see this robust and high-quality immune response, particularly in antigen-specific CD8+ T cells, from a single dose and without any combination therapy. I'm excited to see how these early immunogenicity data may translate to clinical outcomes in the future."

These preliminary immunogenicity data reinforce the promising anti-tumor activity reported from this trial in December 2020 and are consistent with recently published preclinical data, which showed that intravenous HB-201 administration induced single digit percentage of antigen-specific CD8+ T cells, while alternating administration of HB-201 and HB-202 induced a potent CD8+ T cell response, exceeding 50% of the circulating T cell pool. As the HB-201/HB-202 clinical trial is ongoing, HOOKIPA expects to present additional translational and clinical data at upcoming medical conferences in 2021. The company anticipates these data to further inform the HPV program, as well as other earlier stage programs in its oncology pipeline, including therapeutics for prostate cancer, as it seeks to deliver transformational therapies through induction of antigen-specific CD8+ T cells. The poster and audio review are available at https://ir.hookipapharma.com/events/event-details/aacr-annual-meeting-2021.

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 (LCMV for HB-201 and PICV 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 resulted in a ten-fold increase in immune response and better disease control than either compound alone.

About the trial
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. The primary endpoint of the Phase 1 is a recommended Phase 2 dose based on safety and tolerability. Secondary endpoints include anti-tumor activity as defined by RECIST 1.1 and immunogenicity.

The trial is evaluating HB-201 as a single-vector monotherapy, as an alternating two-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. HOOKIPA expects to share interim clinical data on the HB-201/202 therapy in mid-2021.

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 developing a new class of immunotherapeutics based on its proprietary arenavirus platform that reprograms the body's immune system.

HOOKIPA's proprietary arenavirus-based technologies, non-replicating and replicating, induce robust antigen-specific CD8+ T cells and pathogen-neutralizing antibodies. HOOKIPA's viral vectors target antigen presenting cells in vivo to activate the immune system. Both technologies enable repeat administration to augment and refresh immune responses. As a monotherapy not used in combination, our replicating arenavirus technology has the potential to induce CD8+ T cell response levels previously not achieved by other immuno-therapy approaches.

HOOKIPA is building a proprietary immuno-oncology pipeline by targeting virally mediated cancer antigens, self-antigens and next-generation antigens. The lead replicating arenavirus oncology product candidates, HB-201 and HB-202, are in development for the treatment of Human Papilloma Virus 16-positive cancers in a Phase 1/2 clinical trial.

HOOKIPA's non-replicating prophylactic Cytomegalovirus (CMV) vaccine candidate, HB-101, is currently in a Phase 2 clinical trial for patients awaiting kidney transplantation. To expand its infectious disease portfolio, HOOKIPA entered into a collaboration and licensing agreement with Gilead Sciences, Inc. to research arenavirus-based functional cures for HIV and chronic Hepatitis B infections.

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-K for the financial year ended December 31, 2020 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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