



HOOKIPA advances HB-200 program to Phase 2 and prioritizes oncology portfolio based on clinical data updates across its novel arenaviral platform

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- Based on positive interim Phase 1 data, HOOKIPA initiates Phase 2 study to assess HB-201 in combination with pembrolizumab in 1st and 2nd line head and neck cancer
- Interim Phase 1 HB-200 data continue to show high levels of tumor-specific CD8+ T cells, promising early anti-tumor activity (including 75 percent disease control rate, three partial responses and one near partial response), and a favorable tolerability profile in advanced head and neck cancer
- HOOKIPA advancing immuno-oncology pipeline across numerous cancers, including HB-300 for prostate cancer and HB-700 for KRAS-mutated cancers, and evaluating combinations of HB-200 with other oncology treatment modalities
- Interim Phase 2 HB-101 data show consistent immunogenicity, tolerability, and reduction in CMV viremia in kidney transplant patients; HOOKIPA pursuing partnership opportunities for continued development of HB-101

NEW YORK and VIENNA, Austria, Nov. 09, 2021 (GLOBE NEWSWIRE) -- HOOKIPA Pharma Inc. (NASDAQ: HOOK, 'HOOKIPA'), a company developing a new class of immunotherapeutics based on its proprietary arenavirus platform, announced it is advancing HB-201 to Phase 2, to be evaluated in combination with pembrolizumab as 1st- or 2nd-line treatment for Human Papillomavirus Positive 16 (HPV16+) squamous cell head and neck cancers (HNSCC). Interim Phase 1 data in heavily pre-treated patients continue to show HB-200 monotherapy (both HB-201 alone and HB-202/HB-201) is highly effective at expanding T cells, has a favorable tolerability profile and promising, early anti-tumor activity. As of November 1, 2021, among 28 patients dosed intravenously, HB-200 resulted in a 75 percent disease control rate and shrinkage of target lesions in 53 percent of patients. In these patients, HOOKIPA has observed three partial responses (including one confirmed and one unconfirmed in an ongoing patient) and one ongoing patient with a near partial response (29 percent tumor shrinkage). Based on the strength of the HB-200 data, HOOKIPA has prioritized its oncology portfolio and plans further development of its infectious disease programs to be done in partnership with other companies. HOOKIPA will host an investor conference call to review the data at 4:30 p.m. ET.

"We are incredibly excited about our Phase 1 HB-200 data, especially the demonstrated tumor-specific T cell responses and tumor shrinkage in heavily pre-treated HNSCC patients, which we believe are highly differentiated from other active immunization technologies," said Joern Aldag, Chief Executive Officer at HOOKIPA. "Based on these data, we're excited to advance our promising HB-200 program into Phase 2, initially with the HB-201 and pembrolizumab combination for head and neck cancer patients, while accelerating the development of our earlier stage immuno-oncology candidates HB-300 and HB-700 in prostate and KRAS-mutated cancers, respectively, and focusing our efforts on exploring the potential of our novel arenaviral technology to address unmet needs in cancer."

HB-200 data update

Interim data from the ongoing Phase 1 dose escalation study (NCT04180215) show that HB-200 (either as HB-201 or as alternating two-vector HB-202/HB-201) rapidly induces high levels of tumor-specific CD8+ T cells considered to be predictive of response, with a favorable tolerability profile and promising, early anti-tumor activity in heavily pre-treated HPV16+ HNSCC cancer patients.

As of the November 1, 2021 data cut-off, 62 patients (representing 24 new patients since the data presented at the American Society of Clinical Oncology in June 2021) with advanced HPV16+ tumors were enrolled and received HB-200 therapy. Forty patients with HNSCC tumors were treated intravenously every three weeks, including 20 patients who received single vector HB-201 and 20 patients who received alternating two-vector HB-202/HB-201. The other 22 patients had either other HPV16+ tumor types (not HNSCC) and/or received different HB-200 regimens. Participants received a median of three prior therapies (ranging from zero to 11), and 87 percent had previously received a checkpoint inhibitor regimen. The following safety and interim efficacy data reflect the November 1 cut-off date.

Safety results

HB-200 continued to demonstrate a favorable tolerability profile in heavily pre-treated patients with HPV16+ cancers, highlighting its potential in possible combination with checkpoint inhibitors and other agents. Treatment-related adverse events were reported in 66 percent of 62 evaluable patients, with only 8 percent experiencing treatment-related adverse events rated grade 3 or higher.

Interim efficacy results

HB-200 demonstrated promising, early anti-tumor activity in the 28 evaluable patients with advanced HNSCC. Specifically:

- HB-201 showed a 71 percent disease control rate (10/14 evaluable patients, including one confirmed partial response and one unconfirmed partial response, previously reported in December 2020);
- Alternating two-vector HB-202/HB-201 demonstrated a 79 percent disease control rate (11/14 evaluable patients, including one ongoing unconfirmed partial response and one ongoing near partial response with 29 percent tumor shrinkage); and,
- HB-200 showed tumor shrinkage in 53 percent of patients (15/28 evaluable patients) and an ongoing median

progression-free survival (mPFS) of 3.45 months.

These results compare favorably to the standard of care treatments nivolumab and pembrolizumab used in a 2nd plus-line setting in PD1-inhibitor naïve HNSCC patients. Based on peer-reviewed published data, nivolumab showed a mPFS of 2 months¹ whereas pembrolizumab had disease control rates of 35 percent overall and 40 percent in the HPV+ subset in the 2nd plus-line setting.²

T cell data

Interim data continued to show that HB-200 rapidly induces high levels of activated, tumor-specific CD8+ T cells. As of the September 1, 2021 data cut-off, 20 patients were evaluable, including 10 patients who received HB-201 and 10 who received alternating two-vector HB-202/HB-201. The analysis showed:

- More than 90 percent of patients showed an increase in tumor-specific CD8+ T cells within 2 weeks of initial HB-200 dose (either HB-201 or HB-202/HB-201),
- More than 50 percent of patients had tumor-specific CD8+ T cell levels that exceeded the single-digit percentage threshold of the circulating T cell pool, which is generally considered a strong indicator of response; and,
- 50 percent of patients with paired biopsies (3/6 patients) showed elevated tumor infiltrating lymphocytes (“TILs”), or an increase in CD8+ T cells in their tumors.

Based on a review of published literature, we believe that no other active immunization approach has demonstrated these types of results, which highlight the magnitude of tumor-specific CD8+ T cells induced by HB-200 therapy as well as the potential for HOOKIPA's versatile arenaviral platform to enhance anti-tumor activity across tumor killing mechanisms.

“While these T cell data are preliminary, it’s clear that HB-200 induces a rapid and robust vaccine-specific T cell response at magnitudes that we as a field have theorized would result in efficacy, if such levels were ever achieved,” said Dmitriy Zamarin, MD, PhD, Translational Research Director in Gynecologic Medical Oncology at Memorial Sloan Kettering Cancer Center (MSK) and co-investigator in this study. “Hookipa’s arenavirus vectors are, for the first time, generating these levels and, with that, we are seeing monotherapy efficacy in patients with advanced heavily-pretreated cancers.”

Oncology pipeline expansion

There is considerable unmet need in head and neck cancers, and the HB-200 program represents broad potential for additive benefits in combination with current standard of care and novel agents to improve anti-tumor immune response in these patients. HOOKIPA has initiated the Phase 2 expansion portion of its ongoing HB-200 study to evaluate HB-201 in combination with pembrolizumab in 1st- and 2nd-line HNSCC patients.

The company also plans to initiate a separate, randomized Phase 2 study of HB-200 in combination with pembrolizumab as part of its clinical collaboration with Merck & Co., Inc., Kenilworth, NJ, USA.

Based on the positive HB-200 data to-date, HOOKIPA is focusing future research and development in oncology, advancing efforts in head and neck cancer with HB-200 and prostate cancers with HB-300, as well as expanding its pipeline to include HB-700, a new program targeting KRAS-mutated colorectal, pancreatic and lung cancers.

Infectious disease portfolio update

Updated interim data from the ongoing Phase 2 clinical trial (NCT03629080) of HB-101, a prophylactic Cytomegalovirus (CMV) vaccine candidate, show strong immunogenicity and reduced incidence of CMV viremia in people who received three doses of HB-101, consistent with results previously reported in November 2020. Compared to placebo, participants vaccinated with three HB-101 doses prior to kidney transplant had:

- Strong immunogenicity with 86 percent seroconversion and 100 percent CD8+ T cell responses;
- a 41 percent reduction in CMV viremia (presence of CMV DNA in the blood);
- a 41 percent reduction in the use of antiviral therapy; and,
- No change in CMV disease.

While there were two cases of CMV disease reported in the placebo group in November 2020, these cases have since been re-classified as not CMV disease.

Safety and tolerability were evaluated in 80 participants who were enrolled in the trial by the cut-off date of July 30, 2021. HB-101 was generally well tolerated with 21 percent of HB-101 recipients experiencing side effects related to vaccine administration. A total of five cases of human leukocyte antigen (HLA)-sensitization have been reported, four characterized as serious adverse events.

Enrollment closed in June 2021 with 80 patients enrolled, and participants will continue to be monitored for the 12-month observation period following kidney transplantation. Final results are anticipated in 2023. With no approved CMV vaccine, there remains considerable unmet need for people with solid organ transplants. HOOKIPA will explore partnership opportunities for further development of HB-101 in order to focus on advancing its promising oncology portfolio.

HOOKIPA is progressing its research collaboration with Gilead to develop a potential functional cure for Hepatitis B virus (HBV). The HBV program successfully passed Gilead’s Request for Development milestone, and Gilead plans to progress the program into IND-enabling stage in 2022 to support IND filing for the arenavirus vector combination. For the HIV program, after HOOKIPA successfully completed all pre-clinical research obligations in accordance with the mutual Collaboration Agreement, Gilead informed HOOKIPA of their intention not to move forward with this program according to current terms. HOOKIPA is in ongoing discussions with Gilead regarding a revised Collaboration Agreement.

Investor call

HOOKIPA will host an investor conference call to review the data at 4:30 p.m. ET.

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A live webcast of the call can be accessed on HOOKIPA's website at <https://ir.hookipapharma.com/events>. An archived webcast will be available for 30 days on the Events webpage.

About HB-202/HB-201

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 resulted in a ten-fold increase in immune response and better disease control than either compound alone. HB-201 is being tested clinically as a single vector therapy and also in an alternating vector combination with HB-202.

About the HB-200 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+ head and neck cancers who progressed on standard of care, including check point inhibitors. 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. The primary endpoint of 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.

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 to address unmet needs in cancer.

The company is leveraging its proprietary, versatile platform to engineer a broad pipeline of differentiated arenaviral therapeutics. These novel immunotherapies induce robust antigen-specific killer T cells to a broad range of self and non-self antigens, including viral antigens, tumor-associated antigens and neoantigens. HOOKIPA's platform technology uses replicating viral vectors based on the target cancer, with the potential to induce killer T cell response levels previously not achieved by other immunotherapy approaches.

HOOKIPA's pipeline includes wholly-owned investigational arenaviral immunotherapeutics targeting Human Papillomavirus Positive 16, prostate cancer, KRAS-mutated cancers (including colorectal, pancreatic and lung), and other undisclosed projects. In addition, the company aims to develop functional cures of HBV and HIV in collaboration with Gilead.

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

Disclosure: Dr. Zamarin provides consulting services to HOOKIPA Pharma.

Forward Looking Statements

This press release may contain a number of "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements regarding HOOKIPA's expectation about any or all of the following: (i) the success, cost and timing of HOOKIPA's product development activities and clinical trials; (ii) the timing, scope or likelihood of regulatory filings and approvals, including timing of Investigational New Drug Application and Biological Licensing Application filings for HOOKIPA's current and future product candidates, and final U.S. Food and Drug Administration, European Medicines Agency or other foreign regulatory authority approval of HOOKIPA's current and future product candidates; (iii) HOOKIPA's ability to develop and advance its current product candidates and programs into, and successfully complete, clinical studies; (iv) the potential benefits of and HOOKIPA's ability to maintain its collaboration with Gilead Sciences, Inc., and establish or maintain future collaborations or strategic relationships or obtain additional funding; (v) risks relating to business interruptions resulting from the coronavirus (COVID-19) disease outbreak or similar public health crises 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. Forward-looking statements can be identified by terms such as "believes," "expects," "plans," "potential," "would" or similar expressions and the negative of those terms. HOOKIPA has based these forward-looking statements largely on its current expectations and projections about future events and financial trends that it believes may affect its business, financial condition and results of operations. Although HOOKIPA believes that such statements are based on reasonable assumptions, forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond HOOKIPA's control, you should not rely on these forward-looking statements as predictions of future events. These risks and uncertainties include, among others: outcomes of HOOKIPA's planned clinical trials and studies may not be favorable; that one or more of HOOKIPA's product candidate programs will not proceed as planned for technical, scientific or commercial reasons; availability and timing of results from preclinical studies and clinical trials; uncertainty about regulatory approval to conduct clinical trials or to market a products; uncertainties regarding intellectual property protection; and those risk and uncertainties described under the heading "Risk Factors" in HOOKIPA's Form 10-Q for the quarter ended June 30, 2021 filed with the U.S. Securities and Exchange Commission, and in any other subsequent filings made by HOOKIPA with the U.S. Securities and Exchange Commission, which are available at www.sec.gov and HOOKIPA's website at www.hookipapharma.com.

Existing and prospectus investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. HOOKIPA disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this presentation, other than to the extent required by law.

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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¹ Ferris R et al. Nivolumab for recurrent squamous-cell carcinoma of the head and neck. *N Engl J Med.* 2016; 375:1856-1867.

² Mehra R et al. Efficacy and safety of pembrolizumab in recurrent/metastatic head and neck squamous cell carcinoma: pooled analysis after long-term follow up in KEYNOTE-012. *British J of Cancer.* 2018; 119:153-159.