Elevation Oncology Announces the Presentation of New Preclinical Data in Pancreatic and Cholangiocarcinoma PDX Models on the Specific Inhibition of HER3 with Seribantumab to Block NRG1 Fusion Signaling

Results further support the investigation of monotherapy seribantumab for the treatment of solid tumors uniquely driven by an NRG1 fusion in the ongoing Phase 2 CRESTONE study

Data presented at the AACR Virtual Annual Meeting 2021

NEW YORK, NY – April 10, 2021 – Elevation Oncology, a clinical stage biopharmaceutical company focused on the development of precision medicines for patients with genomically defined cancers, announced today the today the presentation by its collaborators in the Marc Ladanyi lab at Memorial Sloan Kettering (MSK) of further preclinical data on the specific inhibition of NRG1 fusion-induced tumorigenesis and signaling by seribantumab, a HER3 monoclonal antibody, at the American Association of Cancer Research Virtual Annual Meeting 2021. These data (Odintsov et al., 2021) in patient-derived xenograft (PDX) models of NRG1 fusion-positive pancreatic and cholangiocarcinoma build on earlier studies generated in lung and ovarian NRG1 fusion PDX models, recently published in Clinical Cancer Research, and further support the mechanistic rationale for the Phase 2 CRESTONE study for patients with solid tumors of any origin harboring an NRG1 gene fusion. The CRESTONE study is currently enrolling at sites across the United States.

"Here we observed that NRG1 fusions activated HER3 and downstream signaling mediators such as AKT in a pancreatic cell line," said Igor Odintsov, MD, Research Fellow at MSK and lead author of the poster presentation. "Treatment with seribantumab was able to inhibit phosphorylation of the activated HER3 and AKT in the same cell line, and subsequent treatment of an APP-NRG1 fusion-positive pancreatic PDX model with seribantumab robustly inhibited tumor growth at clinically achievable doses."

Regressions were observed in all mice treated with 10 mg/kg BIW seribantumab, equivalent to a clinical dose of 2.6 g seribantumab in humans by allometric scaling. As in prior analysis in lung and ovarian NRG1 fusion PDX models, the pan-ERBB inhibitor afatinib was used as an active control in this pancreatic PDX model. No regression was observed in pancreatic PDX tumors treated with afatinib at 5 mg/kg QD.

NRG1 fusions have been identified in a variety of solid tumors, including lung, pancreatic, gallbladder, breast, ovarian, colorectal, neuroendocrine, cholangiocarcinomas, and sarcomas. Current data suggest that NRG1 fusions are predominantly mutually exclusive with other known driver alterations and are therefore considered to be the primary driver of the tumor's growth and proliferation.

"The rarity of competing oncogenic drivers in tumors driven by an NRG1 fusion presents a strong biological rationale for use of a targeted anti-HER3 monotherapy approach across tumor types. This approach is reflected in the design of our Phase 2 CRESTONE study as a tumor-agnostic study of monotherapy seribantumab with pre-defined exclusion of patients whose tumors harbor multiple actionable driver alterations," said Shawn M. Leland, PharmD, RPh, Founder and Chief Executive Officer of Elevation Oncology. "In rare instances when multiple actionable driver alterations are identified in the same tumor, we believe there may be a similar biological rationale for addressing each driver alteration through combinations of agents targeted to each individual alteration, rather than the traditional combinations with chemotherapy. We are excited to report early results from preclinical exploration of this hypothesis, and look forward to continued investigation of new treatment paradigms informed by comprehensive genomic profiling of tumors."

"We utilized an RBPMS-NRG1 fusion cholangiocarcinoma PDX model that also contained mutations in both ERBB4 and IDH1," continued Dr. Odintsov. "While treatment with monotherapy seribantumab or

afatinib in this model produced mixed results, by applying a triple combination of seribantumab with afatinib to target the entire ERBB family, and AG-120 to target the IDH1 mutation, we were able to achieve regressions in the majority of tumors. This suggests that tumors harboring multiple oncogenic drivers may benefit from combination therapy that addresses the contribution of each genomic alteration in disease progression."

In totality, the data reported support the use of monotherapy seribantumab to treat GI and other cancers that are uniquely driven by an NRG1 fusion in the ongoing Phase 2 CRESTONE study. Patients and physicians can learn more about the CRESTONE study at http://www.NRG1fusion.com/ or on www.ClinicalTrials.gov under the NCT number NCT04383210.

About Elevation Oncology
Elevation Oncology is founded on the belief that every patient living with cancer deserves to know what is driving the growth of their disease and have access to therapeutics that can stop it. We aim to make genomic tests actionable by selectively developing drugs to inhibit the specific alterations that have been identified as drivers of tumor growth. Together with our peers, we work towards a future in which each tumor's unique genomic test result can be matched with a purpose-built precision medicine to enable an individualized treatment plan for each patient. Our lead candidate, seribantumab, is intended to inhibit tumor growth driven by NRG1 fusions and is currently being clinically tested in the Phase 2 CRESTONE study for patients with tumors of any origin that have an NRG1 fusion. Details on CRESTONE are available at www.NRG1fusion.com. For more information visit www.ElevationOncology.com.

About Seribantumab and NRG1 Gene Fusions
Seribantumab is a fully human IgG2 monoclonal antibody that binds to human epidermal growth factor receptor 3 (HER3). HER3 is traditionally activated through binding of its primary ligand, neuregulin-1 (NRG1). The NRG1 gene fusion is a rare genomic alteration that combines NRG1 with another partner protein to create chimeric NRG1 "fusion proteins". The NRG1 fusion protein is often also able to activate the HER3 pathway, leading to unregulated cell growth and proliferation. Importantly, NRG1 gene fusions are predominantly mutually exclusive with other known genomic driver mutations and are considered a unique oncogenic driver event associated with tumor cell survival.

NRG1 fusions have been identified in a variety of solid tumors, including lung, pancreatic, gallbladder, breast, ovarian, colorectal, neuroendocrine, cholangiocarcinomas, and sarcomas. In preclinical experiments, seribantumab prevented the activation of HER3 signaling in cells that harbor an NRG1 gene fusion. In addition to extensive nonclinical characterization and testing, seribantumab has been administered to 847 patients across 12 Phase 1 and 2 studies, both as a monotherapy and in combination with various anti-cancer therapies. Seribantumab is currently being evaluated in the Phase 2 CRESTONE study for patients with solid tumors of any origin that have an NRG1 fusion.

About the CRESTONE Study
Clinical Study of Response to Seribantumab in Tumors with Neuregulin-1 (NRG1) Fusions. CRESTONE is a Phase 2 tumor-agnostic "basket trial" of seribantumab in patients with solid tumors that harbor an NRG1 fusion and have progressed after at least one prior line of standard therapy. The primary objective of the study is to describe the anti-tumor activity and safety of seribantumab as a monotherapy specifically in patients whose solid tumor is uniquely driven by an NRG1 fusion. CRESTONE offers a clinical trial opportunity for patients with advanced solid tumors who have not responded or are no longer responding to treatment. Patients are encouraged to talk to their doctor about genomic testing of their tumor. CRESTONE is open and enrolling today in the United States. For more information visit www.NRG1fusion.com.

For further information, please contact:

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