Elevation Oncology Announces Clinical Cancer Research Publication Highlighting the Specific Inhibition of HER3 by Seribantumab in Preclinical NRG1 Fusion Models

- Results show seribantumab efficiently inhibited HER3 and the entire ERBB family signaling pathway and established a biologically effective dose range for tumors driven by an NRG1 fusion -
- Seribantumab is currently being evaluated in the tumor-agnostic Phase 2 CRESTONE trial for patients with any solid tumor harboring an NRG1 fusion -

NEW YORK, April 6, 2021 /PRNewswire/ -- Elevation Oncology, a clinical stage biopharmaceutical company focused on the development of precision medicines for patients with genomically defined cancers, announced today the publication in *Clinical Cancer Research*, a journal of the American Association for Cancer Research, of peer-reviewed data in support of the scientific rationale for the Phase 2 CRESTONE study for patients with solid tumors of any origin that have an NRG1 fusion. The CRESTONE study is currently enrolling at sites across the United States.

The manuscript titled "*The anti-HER3 monoclonal antibody seribantumab effectively inhibits growth of patient-derived and isogenic cell line and xenograft models with oncogenic NRG1 fusions*," can be accessed online here: Odintsov et al., *Clinical Cancer Research* 2021

"With this work, we aimed to expand the biological understanding of NRG1 fusions as an oncogenic driver and the importance of broad inhibition of downstream signaling activated through ERBB family complexes involving HER3 (ERBB3) in tumors driven by NRG1 rearrangements," said Igor Odintsov, MD, Research Fellow, Memorial Sloan Kettering Cancer Center (MSK), lead author, who performed these studies with Romel Somwar, PhD, Senior Research Scientist in the Ladanyi Lab at MSK. "Given that HER3 is required for NRG1 fusion-driven tumor growth but does not have an active kinase domain to directly target with small molecule antagonists, targeting HER3 with an antibody is an attractive therapeutic strategy."

The study results reported in the manuscript suggest that targeted inhibition of HER3 with the anti-HER3 mAb seribantumab is not only able to inhibit ligand-dependent activation by the NRG1 fusion protein but also to de-stabilize the entire subsequent ERBB and downstream signaling pathways that drive tumor growth and proliferation, leading to significant tumor regression of 50 – 100% in NRG1 fusion models. Notably, the entire biologically effective dose range observed in these models of 1 mg BIW – 10 mg BIW seribantumab falls below the equivalent human dosage of seribantumab currently being used in clinical trials. In contrast, similar tumor regression in response to afatinib, a pan-ERBB inhibitor, was only observed at 15 mg/kg QD, above the recommended dose of afatinib for patients based upon allometric scaling.

Seribantumab is currently being clinically evaluated in the tumor-agnostic Phase 2 CRESTONE trial for patients with solid tumors harboring an NRG1 fusion. CRESTONE is currently open and enrolling patients across the United States. The primary objective of the study is to describe the Objective Response Rate (ORR) of seribantumab by independent central radiographic review, and key secondary endpoints are Duration of Response (DoR) and safety.

"We thank our collaborators at MSK for their rigorous evaluation of therapeutic approaches for this rare, genomically defined patient population, and their commitment to developing the novel NRG1 fusion models that enable targeted preclinical investigation of seribantumab," said Shawn Leland, PharmD, RPh, Founder and CEO of Elevation Oncology. "This publication represents the first peer-reviewed data in support of the specific development of seribantumab for patients whose solid tumors are driven by an NRG1 fusion, showing that across these preclinical models of aggressive disease in various tumor types and fusion partners, direct inhibition of HER3 by seribantumab shows potential to generate significant and durable anti-cancer effects at clinically achievable doses."

Patients and physicians can learn more about the CRESTONE study at 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 evaluated in the Phase 2 CRESTONE study for patients with solid 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 trial 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.

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