ALX Oncology Reports ASPEN-03 and ASPEN-04 Phase 2 Trials Evaluating Evorpacept with a Checkpoint Inhibitor for the Treatment of Head and Neck Cancers Did Not Meet Primary Endpoints

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- **In ASPEN-03 and ASPEN-04 trials, efficacy data do not support advancing evorpacept in combination with Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab), into a registrational study**
- **Company remains confident in continuing to pursue evorpacept in multiple clinical trials, based on the different mechanism of evorpacept in combination with anti-cancer antibodies, as evidenced by durable clinical response and consistent safety data in prior clinical trials**

SOUTH SAN FRANCISCO, April 25, 2025 (GLOBE NEWSWIRE) -- ALX Oncology Holdings Inc., ("ALX Oncology" or the "Company") (Nasdaq: ALXO), a clinical-stage biotechnology company advancing a pipeline of novel therapies designed to treat cancer and extend patients' lives, today announced topline data from its Phase 2 ASPEN-03 and ASPEN-04 clinical trials. The company's investigational CD47-blocker evorpacept, when added to Merck's (known as MSD outside of the US and Canada) anti-PD-1 therapy, KEYTRUDA® (pembrolizumab) with or without chemotherapy, did not meet the primary endpoints in the ASPEN-03 and ASPEN-04 trials of improved objective response rates (ORR) as compared to historical controls of pembrolizumab alone and pembrolizumab with chemotherapy, respectively, as a first-line treatment in patients with advanced head and neck squamous cell carcinoma (HNSCC). The combination of evorpacept and pembrolizumab with or without chemotherapy in ASPEN-03 and ASPEN-04 demonstrated a manageable safety profile and was consistent with what has been previously reported for pembrolizumab and chemotherapy in this setting. Although the company will no longer pursue evorpacept in combination with pembrolizumab in HNSCC, multiple clinical trials of evorpacept in combination with anti-cancer antibodies will continue based on established proof-of-concept.

Evorpacept blocks the 'don't eat me' signal transmitted by CD47 on the surface of cancer cells that these cells use to evade detection by the immune system. As its primary mechanism of action, evorpacept is uniquely designed to stimulate macrophages to selectively attack cancer cells and not healthy cells, when combined with active anti-cancer antibodies. This mechanism has translated into durable clinical responses and a well-tolerated safety profile in HER2-positive gastric and HER2-positive breast cancer clinical trials. To further explore the benefit in this setting, evorpacept is currently being evaluated in combination with various anti-cancer antibodies in colorectal cancer, breast cancer, non-Hodgkin lymphoma and multiple myeloma.

In the ASPEN-03 and ASPEN-04 clinical trials, evorpacept was combined with pembrolizumab with or without chemotherapy to investigate a second and distinct mechanism of action. This discrete approach explored the concept that evorpacept may enhance T-cell priming by activating dendritic cells and stimulating the adaptive immune system. The trial outcomes were not sufficiently supportive of advancing evorpacept in combination with pembrolizumab in HNSCC into a registrational trial.

"While there were encouraging trends in ASPEN-03 in ORR versus the historical and internal control, we've decided not to pursue evorpacept and pembrolizumab in head and neck cancer in light of our prioritization of the more established anti-cancer antibody combination program based on multiple positive studies," said Alan Sandler, M.D., Chief Medical Officer at ALX Oncology. "We are disappointed that these studies did not meet their primary endpoints, most importantly for the patients for whom current standard-of-care treatment approaches fall short, and we thank all who participated in the trials."

"Moving forward, we are continuing to rapidly advance our clinical program combining evorpacept with anti-cancer antibodies supported by robust clinical data across trials in multiple tumor types. Evorpacept has demonstrated response rates and durability beyond what is expected from standard of care across several studies when combined with HERCEPTIN®, zanidatamab and RITUXAN®," said Jason Lettmann, Chief Executive Officer at ALX Oncology. "Based on the positive data and strong mechanistic rationale, we maintain our confidence in the evorpacept clinical development program and intend to deliver on that promise with additional clinical data in breast cancer and colorectal cancer in the near-term. With evorpacept and ALX2004, our novel EGFR-targeted antibody-drug conjugate, we continue our commitment to bringing forth meaningful therapies for patients living with cancer."

Detailed findings from the ASPEN-03 and ASPEN-04 trials will be submitted to a future medical meeting.

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

About ASPEN-03 and ASPEN-04 Clinical Trials
ASPEN-03 and ASPEN-04 are randomized, multi-center, international Phase 2 trials evaluating evorpacept, ALX Oncology's

investigational CD47-blocking therapeutic that uniquely combines a high-affinity CD47-binding domain with an inactivated proprietary Fc domain, in patients with metastatic or unresectable, recurrent HNSCC who have not yet been treated for their advanced disease. The ASPEN-03 trial (NCT04675294) is evaluating evorpacept in combination with Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab) against pembrolizumab alone for the treatment of patients whose HNSCC is PD-L1 positive. The ASPEN-04 trial (NCT04675333) is evaluating evorpacept in combination with pembrolizumab and chemotherapy against pembrolizumab and chemotherapy alone in patients with HNSCC, regardless of PD-L1 status. Patient characteristics in the trials (N=346) were generally well-balanced across arms. The primary endpoints for the ASPEN-03 and ASPEN-04 trials is ORR compared to historical control. Key secondary endpoints for both trials are safety, duration of response (DOR), progression-free survival (PFS) and overall survival (OS).

About Head and Neck Squamous Cell Carcinoma (HNSCC)
HNSCC is a serious and life-threatening disease that originates in the squamous cells lining the mucosal surfaces of the head and neck, including the mouth, throat, voice box, sinuses and nasal cavity. HNSCC is the seventh most common cancer worldwide and the incidence of HNSCC is expected to increase 30% by 2030. Despite current standard-of-care therapies and recent advancements in diagnosis and treatment, people with HNSCC face a poor prognosis, particularly when diagnosed at advanced stages. Further, the survival rate for HNSCC has only modestly improved in recent years, even with the availability of new treatment modalities, underscoring a need for improved therapeutics.

About Evorpacept
ALX Oncology's lead therapeutic candidate, evorpacept, is a highly differentiated potential best- and first-in-class CD47 checkpoint inhibitor and one of the most advanced checkpoint inhibitors to target and activate the innate immune system. Evorpacept was intentionally designed to maximize the clinical potential of blocking CD47, while reducing the toxicities associated with previous approaches to CD47 blockade. In clinical studies across a wide spectrum of tumor types in more than 700 patients to date, evorpacept has demonstrated potential to enhance the therapeutic activity of many of the most important cancer therapies available today, contributing an additional, differentiated immuno-oncology mechanism. Based on this potential, ALX Oncology is advancing a robust clinical program evaluating evorpacept in a wide range of cancer indications, prioritizing its combination with anti-cancer antibodies in breast, gastric and colon cancers. The U.S. Food and Drug Administration (FDA) has granted Fast Track designation to evorpacept for the second-line treatment of patients with HER2-positive gastric or GEJ carcinoma. Additionally, both the FDA and European Commission have granted Orphan Drug Designation for this indication.

About ALX Oncology
ALX Oncology (Nasdaq: ALXO) is a clinical-stage biotechnology company advancing a pipeline of novel therapies designed to treat cancer and extend patients' lives. ALX Oncology's lead therapeutic candidate, evorpacept, has demonstrated potential to serve as a cornerstone therapy upon which the future of immuno-oncology can be built. Evorpacept is currently being evaluated across multiple ongoing clinical trials in a wide range of cancer indications. ALX Oncology's second pipeline candidate, ALX2004, is a novel EGFR-targeted antibody-drug conjugate with a differentiated mechanism of action and is anticipated to enter Phase 1 trials mid-2025. More information is available at www.alxoncology.com and on LinkedIn @ALX Oncology.

Cautionary note regarding forward-looking statements
This press release contains forward-looking statements that involve substantial risks and uncertainties. Forward-looking statements include statements regarding future results of operations and financial position, business strategy, product candidates, planned preclinical studies and clinical trials, results of clinical trials, research and development costs, regulatory approvals, timing and likelihood of success, plans and objects of management for future operations, as well as statements regarding industry trends. Such forward-looking statements are based on ALX Oncology's beliefs and assumptions and on information currently available to it on the date of this press release. Forward-looking statements may involve known and unknown risks, uncertainties and other factors that may cause ALX Oncology's actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. These and other risks are described more fully in ALX Oncology's filings with the Securities and Exchange Commission (SEC), including ALX Oncology's Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and other documents ALX Oncology files with the SEC from time to time. Except to the extent required by law, ALX Oncology undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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