ALX Oncology Announces First Patients Dosed with Evorpacept and Sarclisa As Part of Randomized Phase 1/2 UMBRELLA Study with Sanofi

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Clinical study is evaluating ALX Oncology's investigational CD47-blocking therapeutic with Sanofi's approved CD38 monoclonal antibody in patients with multiple myeloma

SOUTH SAN FRANCISCO, Calif., Sept. 04, 2024 (GLOBE NEWSWIRE) -- ALX Oncology Holdings Inc., ("ALX Oncology" or "the Company") (Nasdaq: ALXO), an immuno-oncology company developing therapies that block the CD47 immune checkpoint pathway, announced the first patients have been dosed in an arm of the randomized UMBRELLA phase 1/2 clinical study partnered with Sanofi that is evaluating evorpacept in combination with SARCLISA® (isatuximab-irfc). Evorpacept is ALX Oncology's investigational CD47-blocking therapeutic that uniquely combines a high-affinity CD47-binding domain with an inactivated Fc domain and SARCLISA is Sanofi's approved CD38 monoclonal antibody in patients with relapsed or refractory multiple myeloma (RRMM).

SARCLISA binds to a specific epitope on the CD38 receptor on multiple myeloma (MM) cells, inducing distinct antitumor activity. CD38 is highly and uniformly expressed on the surface of MM cells and after first-line treatment, some relapsed or recurred patients have shown resistance to CD38 agents. CD47 expression increases as multiple myeloma progresses, suggesting that evorpacept may have the potential to re-sensitize tumors to CD38 treatment or overcome anti-CD38 resistance. This novel therapeutic combination has demonstrated synergistic anti-tumor activity in preclinical models.

"Multiple myeloma remains an incurable hematologic malignancy for which there is significant need for innovation in new treatment modalities to improve the clinical management of this disease," said Sophia Randolph, M.D., Ph.D., Chief Medical Officer at ALX Oncology. "We are excited by the potential for the therapeutic combination being evaluated in the UMBRELLA study, in collaboration with Sanofi, to improve patient outcomes. This trial also reinforces the significant potential of evorpacept to deepen anti-cancer activity while maintaining a strong safety profile in combination with a range of therapeutic regimens used to treat both hematologic and solid cancers."

Under the terms of the agreement, Sanofi will conduct the multicenter, randomized, open-label, controlled, parallel-group UMBRELLA phase 1/2 clinical study (NCT04643002) to evaluate the safety, efficacy, pharmacokinetics and biomarker data of evorpacept in combination with SARCLISA and dexamethasone in patients with RRMM. Part 1 of the study is designed to evaluate the dosing of evorpacept in combination with standard doses of SARCLISA and dexamethasone to identify a recommended evorpacept dose. Part 2 is designed to investigate the efficacy and safety of this three-drug combination in an expanded population of patients with RRMM. ALX Oncology will supply evorpacept and Sanofi will conduct the clinical trial. ALX Oncology owns worldwide commercial rights to evorpacept.

"Our current experience with SARCLISA suggests it may prove to be an excellent combination partner for novel agents in development," said Peter C. Adamson, M.D., Global Head of Oncology Development at Sanofi. "Therefore, we are pleased to share we have started to enroll patients on this arm of our umbrella study. The partnership with ALX Oncology is part of our strategic approach of exploring potentially synergistic combinations to address therapeutic challenges in patients with relapsed or refractory multiple myeloma."

About multiple myeloma
Multiple myeloma (MM) is the second most common hematologic malignancy, with more than 185,000 new diagnoses of MM worldwide annually (Globocan) and over 35,000 new diagnoses in the United States each year (American Cancer Society). Despite available treatments, MM remains an incurable malignancy and is associated with significant patient burden. Since MM does not have a cure, most patients will relapse. Relapsed MM is the term for when the cancer returns after treatment or a period of remission. Refractory MM refers to when the cancer does not respond or no longer responds to therapy.

About ALX Oncology
ALX Oncology is a publicly traded, clinical-stage immuno-oncology company focused on helping patients fight cancer by developing therapies that block the CD47 immune checkpoint inhibitor and bridge the innate and adaptive immune system. ALX Oncology's lead product candidate, evorpacept, is a CD47 blocking therapeutic that combines a high-affinity CD47-binding domain with an inactivated, proprietary Fc domain. To date, evorpacept has been dosed in over 500 subjects and has demonstrated promising activity and favorable tolerability profile across a range of hematologic and solid malignancies in combination with various leading anti-cancer antibodies. ALX Oncology is currently focusing on combining evorpacept with anti-cancer antibodies, antibody-drug conjugates (ADCs), and PD-1/PD-L1 immune checkpoint inhibitors.

Evorpacept's unique profile: anchored by a rational design and triple development pillars
Rationally engineered with an inactive Fc effector function, evorpacept's clinical data to date have demonstrated a substantially improved safety profile over other anti-CD47 molecules in the clinic with an active Fc (i.e., binding the Fc gamma receptor on macrophages). This best-in-class safety profile allows for higher dosage with minimal overlapping toxicity in the combination treatment setting. CD47 expressed on cancer cells binds to its receptor SIRP alpha, which is predominantly expressed on two cell types: macrophages and dendritic cells. The Company's pipeline of therapeutic candidates with standard-of-care agents include:

- **Anti-cancer antibodies and ADCs (the "*don't eat me*" signal):** evorpacept enables Fc-mediated antibody-dependent phagocytosis by macrophages in combination with anti-cancer antibodies (e.g., HERCEPTIN®) and ADCs (e.g., PADCEV® and ENHERTU®) with an active Fc domain, which is otherwise impaired by CD47 expression on cancer cells binding to SIRP alpha on macrophages. Additionally, ADCs target the delivery of a chemotherapeutic payload to tumor cells to exert cytotoxic effects.
- **PD-1/PD-L1 immune checkpoint inhibitors (the "*don't activate T-cells*" signal)**: evorpacept enables T-cell activation by dendritic cells that are constitutively inhibited by CD47 expression on cancer cells binding to SIRP alpha on dendritic cells. Activated dendritic cells present neoantigens to T cells that once activated will kill cancer cells when the PD-1/PD-L1 inhibitory interaction is blocked by T-cell checkpoint inhibitors.

About SARCLISA
SARCLISA (isatuximab-irfc) is a monoclonal antibody that binds to a specific epitope on the CD38 receptor on MM cells, inducing distinct antitumor activity. It is designed to work through multiple mechanisms of action including programmed tumor cell death (apoptosis) and immunomodulatory activity. CD38 is highly and uniformly expressed on the surface of MM cells, making it a target for antibody-based therapeutics such as SARCLISA. SARCLISA is approved in more than 50 countries, including the US and the EU, in combination with pomalidomide and dexamethasone for the treatment of patients with RRMM who have received ≥2 prior therapies, including lenalidomide and a proteasome inhibitor and who progressed on last therapy. SARCLISA is also approved in 50 countries in combination with carfilzomib and dexamethasone, including in the US for the treatment of patients with RRMM who have received 1–3 prior lines of therapy and in the EU for patients with MM who have received at least one prior therapy. SARCLISA continues to be evaluated in multiple ongoing phase 3 clinical studies in combination with current standard treatments across the MM treatment continuum. It is also under investigation for the treatment of other hematologic malignancies, and its safety and efficacy have not been evaluated by any regulatory authority outside of its approved indication.

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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