AIM ImmunoTech Provides Summary of Ampligen® Data Supporting Synergistic Potential with Checkpoint Blockade Therapies

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Ampligen has demonstrated in pre-clinical and now human clinical studies a potential to enhance efficacy of PD-1 and/or PD-L1 checkpoint inhibitors

Ampligen's anti-tumor potential is demonstrated with checkpoint blockade therapies in human clinical studies for the treatment of triple-negative breast cancer and advanced recurrent ovarian cancer

Based on a growing body of clinical data, the Company believes in the potential to expand Ampligen development into treatment of solid tumors

OCALA, Fla., April 21, 2022 (GLOBE NEWSWIRE) -- **AIM ImmunoTech Inc. (NYSE: American AIM)** ("AIM" or the "Company"), an immuno-pharma company focused on the research and development of therapeutics to treat multiple types of cancers, immune disorders, and viral diseases, including COVID-19, the disease caused by the SARS-CoV-2 virus, today provided a summary of clinical data that support the synergistic potential of Ampligen® (rintatolimod) with checkpoint blockade therapies.

Thomas Equels, Chief Executive Officer of AIM, commented, "We have amassed a growing body of encouraging Ampligen data to date through close collaborations with leading KOLs at preeminent institutions. These data have not only affirmed but significantly evolved our belief that Ampligen as a single agent therapy, as well as in combination with the latest powerful cancer therapies, has the potential to become a breakthrough therapy for some of the most difficult to treat and deadly cancers. We are going to continue working tirelessly to advance Ampligen towards approval and commercialization with the goal of bringing much needed hope to patients and solutions to treating physicians around the world."

Ampligen is the Company's dsRNA drug currently being developed for globally important cancers. Ampligen has shown therapeutic synergy with checkpoint inhibitors, including increasing survival rates and efficacy, in the treatment of animal tumors when used in combination with checkpoint blockade therapies. The first detection of Ampligen's synergistic potential with checkpoint blockade therapeutics was witnessed in pre-clinical mouse models of melanoma and pancreatic cancers. Additionally, the Company now has data from two clinical studies - in advanced recurrent ovarian cancer and triple negative breast cancer - that indicate that the drug may have similar anti-tumor activity in humans.

"Working with AIM, our Pancreatic Cancer R&D team at the Buffett Cancer Center did extensive pre-clinical research demonstrating in animal models that Ampligen had a significant therapeutic benefit in treating pancreatic cancer. This March, Prof. C.H.J. van Eijck and his team at Erasmus MC published data in the journal *Cancers* showing Ampligen alone was associated with extended overall survival in late-stage pancreatic cancer of 19 months. Just last week, at AACR, publications of clinical data by UPMC's Dr. Bob Edwards in advanced recurrent ovarian cancer, and Roswell's Dr. Pawel Kalinski in both stage 4 triple negative breast cancer and stage 4 colorectal cancer, strongly supported the advance of Ampligen into human trials for patients in pancreatic and other cancers where checkpoint drugs are not effective," stated Michael (Tony) Hollingsworth, PhD, Associate Director, Basic Research, University of Nebraska Medical Center.

"Checkpoint drugs are powerful and important therapies, but only work on 'hot' tumors visible to the immune system, not 'cold' tumors that are immune-silent. Ampligen appears, from these data, to turn cold tumors into hot tumors and create significant therapeutic potential for a successful second round of Ampligen plus checkpoint therapy for those who do not respond to checkpoint therapy alone," added Robert Edwards, MD, University of Pittsburgh School of Medicine and University of Pittsburgh Cancer Institute.

"The two ongoing Roswell Park clinical trials we recently presented findings from represent milestones in our 10-year-long NIH and DoD-funded research program aiming to convert immuno-resistant 'cold' tumors into 'hot' ones that would be more sensitive to immunotherapy. Seeing both studies successfully meet their predetermined efficacy endpoint - selective increase of cytotoxic T lymphocyte markers in tumor tissues - Roswell Park plans to move forward with critical studies assessing therapeutic efficacy of the combination of a rintatolimod-based chemokine-modulating regimen with PD-1 inhibitors, cancer vaccines and/or adoptive T cell therapies in solid tumors. Observations from our preclinical studies suggest that this multipronged strategy may benefit patients with multiple solid-tumor lesions, which are difficult to target individually," commented Pawel Kalinski, MD, PhD, Jacobs Family Endowed Chair of Immunology, Chief of the Division of Translational Immuno-Oncology and Senior Vice President for Team Science at, Roswell Park Comprehensive Cancer Center.

Recurrent Ovarian Cancer: ClinicalTrials.gov: NCT03734692

The investigator-initiated, Phase 2, single-arm, efficacy/safety trial to evaluate the effectiveness of combining intensive locoregional intraperitoneal (IP) chemoimmunotherapy of cisplatin with IP Ampligen (TLR-3 agonist) and IV infusion of the checkpoint inhibitor pembrolizumab (KEYTRUDA®) (IVP) for patients with recurrent platinum-sensitive ovarian cancer is being conducted by the University of Pittsburgh Medical Center (UPMC). The Phase 2 trial is designed to enroll up to 45 subjects using Ampligen in combination with pembrolizumab to test the combinational activity of checkpoint blockade therapy where Ampligen is administered by injection in the peritoneal cavity where the tumor is located.

The Company's recently announced positive interim results suggesting induction of T cell activation together with clinical responses may indicate prognostic evidence of tumor environment reprogramming that we do not see with chemotherapy alone and which may extend survival. A total of 17 patients have been enrolled and 13 were evaluable for response in the ongoing Phase 2 trial. The observed clinical responses were: 2 complete responses (15.4%), 3 partial responses (23.1%), 3 stable disease (23.1%), 5 progressions (38.4%) for a clinical benefit rate (CR+PR+SD) of 61.6%. From 13 patients, 77 IP wash samples were collected at serial time points. Measurements in IP washes revealed an acute increase in granzyme B (GZMB), perforin, TNF alpha, CXCL9, CXCL10 and CXCL11 after treatment ($p<0.05$). Longitudinal data revealed a progressive increase in some biomarkers in the locoregional environment; CXCL9, CXCL10, CXCL11, perforin and TNF alpha were all increased from baseline levels at cycle 1 to baseline of cycle 6 ($p<0.05$). CXCL12 was also increased acutely after treatment ($p<0.05$).

The cytokine CXCL12 observed to increase acutely after treatment functions as a chemotactic for lymphocytes. The cytokines CXCL9-11 active in antitumor responses in modulation of the tumor microenvironment (TME) to favor cytotoxic T cells required for anti-tumor cell immune activity versus regulatory T cells (Tregs), which function to protect non-tumor "self" tissue. Granzymes are serine proteases released by cytoplasmic granules within cytotoxic T cells and natural killer (NK) cells. They induce programmed cell death (apoptosis) in the target cell, eliminating cells that have become cancerous. Perforin is a protein, which creates tubules in the cell membrane allowing cell lysis. Perforin is a key effector molecule for T-cell- and natural killer-cell-mediated cytolysis.

Triple Negative Breast Cancer: ClinicalTrials.gov: NCT03599453

A Phase 1 study was conducted at Roswell Park Comprehensive Cancer Center in patients with metastatic triple-negative breast cancer using chemokine

modulation therapy, including AIM ImmunoTech Inc.'s drug candidate, Ampligen®, as well as interferon α-2b and pembrolizumab.

In the study, six evaluable patients (33-75 years) with mTNBC received 6 doses of Ampligen (200 mg i.v.), IFN α-2b (INTRON-A; 20MU/m2 i.v.) and COX-2 inhibitor (celecoxib; 2 x 200 mg, p.o.) over 2 weeks, with tumor biopsies obtained before (within 6 days) and after (within 5 days) CKM. All patients received follow-up pembrolizumab (200 mg, i.v, Q3 weeks). Uniform increase of immune markers upon treatment was observed: CD8 mRNA (6.1-fold; p-0.034), GZMB mRNA (3.5-fold; p=0.058), ratios of CD8 /FOXP3 and GZMB/FOXP3 (5.7-fold; p=0.036, and 7.6-fold; p=0.024 respectively), thus successfully meeting the pre-determined primary endpoint in the study (increase in CD8 in TME). In addition, an increase in CTL attractants CXCL10 (2.6-fold; p=0.104) and CCL5 (3.3-fold; p=0.019) was observed. In contrast, Treg marker FOXP3 or Treg attractants CCL22 or CXCL12 were not enhanced. Three patients had stable disease lasting 2.4, 2.5 and 3.8 months, as of data cut off September 1, 2021. An additional patient (non-evaluable) had a partial response (breast tumor autoamputation) with massive tumor necrosis in the post-CKM biopsy.

Results from this proof-of-concept study indicated that short-term systemic chemokine modulating regimen (CKM) followed by pembrolizumab is generally well tolerated and selectively enhances local cytotoxic T-lymphocytes (CTLs) infiltration in the tumor microenvironment (TME), providing rationale for concurrent CKM and PD1 blockade in prospective Phase 2 studies.

Based on the pre-clinical and human clinical data seen to-date, the Company believes Ampligen has the potential to expand into treatment of solid tumors.

About AIM ImmunoTech Inc.

AIM ImmunoTech Inc. is an immuno-pharma company focused on the research and development of therapeutics to treat multiple types of cancers, immune disorders, and viral diseases, including COVID-19, the disease caused by the SARS-CoV-2 virus.

For more information, please visit www.aimimmuno.com.

Cautionary Statement

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 (the "PSLRA"). Words such as "may," "will," "expect," "plan," "anticipate" and similar expressions (as well as other words or expressions referencing future events or circumstances) are intended to identify forward-looking statements. Many of these forward-looking statements involve a number of risks and uncertainties. Among other things, for those statements, the Company claims the protection of safe harbor for forward-looking statements contained in the PSLRA. The Company does not undertake to update any of these forward-looking statements to reflect events or circumstances that occur after the date hereof. Many of the studies discussed above were proof of concept and will require further studies. Studies and trials are subject to many factors including lack of regulatory approval(s), lack of study drug, or a change in priorities at the institutions sponsoring other trials. Significant additional testing and trials will be required to determine whether Ampligen will be an effective treatment of cancer or otherwise, and no assurance can be given that this will be the case.

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