Gradalis Announces Publication in Clinical Cancer Research Featuring Positive Results from a Study Evaluating Vigil® in Combination Therapy for Patients with Recurrent Ewing's Sarcoma

-Pilot study in Ewing's Sarcoma supports the therapeutic potential of Vigil in multiple solid tumor types-

-Circulating tumor DNA levels, used to monitor therapeutic response, corresponded to changes in disease burden-

-Vigil in combination with temozolomide/irinotecan had a favorable safety and tolerability profile-

DALLAS, March 14, 2023 (GLOBE NEWSWIRE) -- Gradalis, Inc., a privately held, late-stage clinical biotechnology company developing a personalized immunotherapy called Vigil® for patients with ovarian and other cancer tumor types, today announced that data from a pilot study evaluating Vigil in combination therapy for the management of recurrent Ewing's Sarcoma was published online in *Clinical Cancer Research*. Study results demonstrated the efficacy of Vigil in combination with temozolomide/irinotecan (TEM/IRI) in recurrent Ewing's patients who had failed prior TEM/IRI treatment. In this study, changes in circulating tumor DNA (ctDNA) levels, an assessment used to monitor therapeutic response, corresponded to changes in disease burden. Furthermore, the combination of Vigil/TEM/IRI had a favorable safety and tolerability profile. These results build on Gradalis' earlier Phase 1 studies involving 19 solid tumor types, as well as the Phase 2a and Phase 2b studies in patients with ovarian cancer, which have all shown positive activity in solid tumors. Vigil is a novel, personalized cellular immunotherapy platform that is designed to decloak the full repertoire of a patient's tumor antigens, reactivate the immune system, and summon key effector cells, like T cells, to deliver a durable clinical response.

"While treatment options for recurrent or refractory Ewing's Sarcoma are limited, we are encouraged by the potential of Vigil in combination with TEM/IRI to contribute to antitumor activity and address the unmet need for these patients," John Nemunaitis, M.D., Chief Scientific Officer of Gradalis. "Results in this publication demonstrated the efficacy of Vigil in combination with TEM/IRI, which was highlighted by corresponding changes in ctDNA levels. This builds on our previous research involving multiple recurrent disease patients who achieved 75% one-year survival compared to historical expected survival of only 23%. Together with the growing safety data, results support future evaluation of Vigil-based combinations in multiple solid tumor types and use of sensitivity biomarkers to track disease response. We look forward to further utilizing ctDNA assessment tools in our Ewing's Sarcoma investigation and beyond."

Key takeaways in the paper include:

- Overview: This was a pilot study of Vigil in combination with TEM/IRI in patients with recurrent or refractory Ewing's Sarcoma. Eight of 10 enrolled patients were evaluable for safety and efficacy, two did not receive Vigil. Seven of eight patients previously received TEM/IRI.
- Efficacy: Observed two partial response (PR) patients by RECIST, both showed histological complete response (CR) without additional cancer therapy at long term follow up. Median PFS was 8.2 months (95% CI, 4.3-NA).
    - Five of eight patients showed stable disease (SD) or better for ≥ 6 months.
    - Patient specific EWS/FLI1 ctDNA was detectable in all eight evaluable patients at baseline.
    - Changes in ctDNA levels corresponded to changes in disease burden.
- Safety: No Vigil-related ≥ Grade 3 adverse events were reported.

About Ewing's Sarcoma

Ewing's Sarcoma is a malignant tumor of the bone and surrounding soft tissues occurring predominantly in young adults. It is classified as a peripheral neuroectodermal tumor (PNET) and is defined by specific chromosomal

translocations resulting in gene fusions of EWSR1 with FLI1, ERG, and other transcription factors. Five year overall survival for patients receiving standard of care with recurrent metastatic Ewing's Sarcoma is less than 15%. Median overall survival with temozolomide/irinotecan approaches 12 months but is typically much lower after failure of this approach.

About Gradalis, Inc.
Gradalis is a privately held, late-stage clinical biotechnology company developing a personalized immunotherapy called Vigil, that has been tested in multiple studies in ovarian and other cancer tumor types. The company has received clearance from the FDA to initiate a Phase 3 trial designed for product registration of Vigil in patients with advanced ovarian cancer. Vigil is the first cellular immunotherapy to demonstrate survival benefits in a randomized controlled trial of ovarian cancer patients. The results of the company's Phase 2b trial have been published in Lancet Oncology and presented at the American Society of Clinical Oncology. Vigil is being studied in other cancer types and has shown positive results in combination with checkpoint inhibitors.

Gradalis' Vigil platform uses the patient's immune system to target the entire tumor. Based on multiple clinical studies, Gradalis has developed an oncology platform that is designed to decloak the full repertoire of a patient's tumor neoantigens, reactivate the immune system, and summon key effector cells to deliver a durable clinical response. When combined, these are a powerful Trifecta of anti-cancer activities, potentially eliminating even the elusive metastatic cells, and as shown in Phase 2 clinical studies in ovarian cancer, a potential gamechanger in oncology. Clinical trials of Vigil have also demonstrated that Gradalis' platform is better tolerated compared to standard cancer treatments since Vigil uses the patient's immune system operating within its natural state of balance rather than in an artificial overdrive as with some technologies. Vigil utilizes proprietary bi-shRNA technology that has been proven to silence multiple genes in a variety of cancers and has the potential to be used in other diseases.

About Vigil
Vigil® is a novel, personalized immunotherapy platform designed to achieve a Trifecta of immune anticancer activity using a unique bi-shRNA DNA based plasmid and the patient's own tumor tissue. The Trifecta of systemic activity involves knock down of TGFβ1 and TGFβ2 which function as tumor suppressor cytokines, increased GM-CSF expression to enhance local immune function and presentation of the patient's clonal neoantigen epitopes via use of autologous cancer tissue. By utilizing the patient's own tumor as the antigen source, Vigil is designed to elicit an immune response that is specifically targeted and broadly relevant to each patient's unique "clonal" tumor neoantigens. Vigil therapy has been well tolerated in Phase 1, 2a and 2b clinical studies.

In VITAL, a multicenter, randomized, double-blind, placebo-controlled Phase 2b trial (NCT02346747), Vigil showed a positive trend in the primary endpoint of recurrence free survival (RFS) in the overall population and a statistically significant improvement in RFS and overall survival (OS), with a median time of three years to date, in a pre-planned subgroup analysis of Stage III/IV newly diagnosed ovarian cancer patients with the BRCAwt molecular profile. In patients with tumors of the HRP type, significant additional improvement was seen in RFS and OS.

Additionally, Phase 1 results in a "basket" clinical trial have shown positive signals of activity in 19 tumor types and some patients treated with Vigil remain in the trial 48 months later. The company is preparing to initiate a clinical trial intended for product registration in patients with the HRP subtype ovarian cancer.

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