RAPT Therapeutics to Report Promising Preclinical Studies Supporting its Pipeline of Immunotherapy Platforms at AACR

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- *Tumor model data shows potential of CCR4 antagonist to alter immunosuppressive tumor microenvironment to improve CAR T-cell therapy in solid tumors*
- *Small-molecule HPK1 inhibitors enhance antitumor immunity in tumor model*
- *Inhibiting GCN2 stress kinase shows potential to restore immunity in tumor microenvironment*

SOUTH SAN FRANCISCO, Calif., March 10, 2021 (GLOBE NEWSWIRE) -- RAPT Therapeutics, Inc. (Nasdaq: RAPT), a clinical-stage, immunology-based biopharmaceutical company focused on discovering, developing and commercializing oral small molecule therapies for patients with significant unmet needs in oncology and inflammatory diseases, today announced several upcoming preclinical poster presentations at the American Association for Cancer Research annual meeting demonstrating promise and potential of its pipeline of anti-cancer agents.

"Our posters at AACR reflect our continued exploration into the role of the immune system in cancer and the potential of immunology-based therapies to address certain challenges in oncology," said Dirk Brockstedt, Ph.D., Chief Scientific Officer of RAPT. "Specifically, the role and importance of CCR4 inhibition will be highlighted and continue to support the early clinical data we have observed with FLX475, our CCR4 inhibitor being evaluated in a Phase 1/2 trial in multiple tumors. In addition, we will also present preclinical data on two exciting next-generation immune-oncology targets, HPK1 and GCN2, which show that orally available inhibitors elicit potent antitumor immune responses in a variety of cancer models."

Summaries of the studies to be presented:

Poster: 1585
Title: T-regulatory cells impair CAR T-cell-mediated antitumor activity in a murine solid tumor model
Session Title: Combination Immunotherapies

Chimeric antigen receptor (CAR) T cell immunotherapy has had only modest success in solid malignancies due in part to tumor antigen heterogeneity and the immunosuppressive tumor microenvironment, which is believed to be at least in part due to immunosuppressive regulatory T cells (T_{reg}). T_{reg} express CCR4 and migrate toward CCL17 and CCL22 which are frequently upregulated in a subset of tumors or increased following immunotherapy. In a murine mesothelioma model, a combination of CAR- T-cells plus CCR4 antagonist significantly slowed tumor growth and significantly improved survival compared to untreated control. Furthermore, enhanced antitumor activity was observed with the combination of CAR T cells and CCR4 antagonist compared to either monotherapy, with 4/9 mice treated with the combination becoming tumor free and experienced significantly increased survival.

Poster: 1646
Title: Development of small-molecule HPK1 inhibitors to unleash tumor-specific T cell responses
Session Title: Immune Checkpoints

Hematopoietic progenitor kinase 1 (HPK1) is an intracellular protein kinase that is associated with inhibition of critical immune T cell signaling and proliferation important for mounting an effective immune response against tumor cells. RAPT's small-molecule compounds demonstrated potent inhibition of HPK1 in biochemical assays, reduction of levels of phosphorylated SLP76 and concomitant increase in IL-2 production. In addition, the Company's HPK1 inhibitors enhanced cytokine production of human and mouse primary T cells above that observed with T-cell receptor activation alone. Notably, treatment of mice with an orally available HPK1 inhibitor resulted in increased activation of antigen-specific CD8 T-cells and decreased tumor growth as monotherapies and in combination with clinically relevant checkpoint inhibitor antibodies.

Poster: 3153
Title: Targeting the stress response kinase GCN2 to restore immunity in the tumor microenvironment
Session Title: Tumor Microenvironment

Recent advances in cancer metabolism suggest that targeting amino acid metabolism represents a promising strategy for the development of novel therapeutic agents. Tumor, stromal and myeloid-derived suppressor cells (MDSC) within the tumor microenvironment (TME) create a nutrient-poor environment that inhibits immune function and support tumor growth. GCN2 (general control nonderepressible 2), a stress response kinase, plays a key role in maintaining cellular homeostasis under a wide range of stressors, leading to T cell anergy, apoptosis, enhanced MDSC-dependent immune suppression and tumor cell survival. The treatment of nutrient-deprived T cells in vitro with a GCN2 inhibitor enhanced CD4 and CD8 T-cell proliferation and effector functions. The GCN2 inhibitor also reversed T cell suppression mediated by MDSCs derived from healthy donors or cancer patients. In syngeneic mouse tumor models, oral administration of a GCN2 inhibitor showed impressive drug-target engagement and potently inhibited GCN2 kinase in the tumor microenvironment. Furthermore, the GCN2 inhibitor as a single agent and in combination with checkpoint inhibitors and

angiogenesis inhibitor (anti-VEGFR) delayed tumor growth in renal cell carcinoma and lung cancer syngeneic tumor models.

About RAPT Therapeutics, Inc.
RAPT Therapeutics is a clinical stage immunology-based biopharmaceutical company focused on discovering, developing and commercializing oral small molecule therapies for patients with significant unmet needs in oncology and inflammatory diseases. Utilizing its proprietary discovery and development engine, the Company is developing highly selective small molecules designed to modulate the critical immune drivers underlying these diseases. RAPT has discovered and advanced two unique drug candidates, FLX475 and RPT193, each targeting C-C motif chemokine receptor 4 (CCR4), for the treatment of cancer and inflammation, respectively. The Company is also pursuing a range of targets that are in the discovery stage of development.

Forward-Looking Statements
This press release contains forward-looking statements. These statements relate to future events and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future performances or achievements expressed or implied by the forward-looking statements. Each of these statements is based only on current information, assumptions and expectations that are inherently subject to change and involve a number of risks and uncertainties. Forward-looking statements include, but are not limited to, statements about the significance of early results from the Phase 1/2 clinical trials of FLX475 and preclinical studies of HPK1 and GCN2, and statements about the potential of CCR4, HPK1 and GCN2 to enhance antitumor activity. Detailed information regarding risk factors that may cause actual results to differ materially from the results expressed or implied by statements in this press release may be found in RAPT's most recent Form 10-Q filed with the Securities and Exchange Commission and subsequent filings made by RAPT with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof. RAPT disclaims any obligation to update these forward-looking statements.

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