RAPT Therapeutics Reports Positive Initial Data from Ongoing Phase 1/2 Clinical Trial of FLX475 in Multiple Cancer Indications

November 16, 2020

-Evidence of Monotherapy and Combination Activity in Charged Tumor Types-
-Company Advances Several Cohorts into Phase 2 Expansions-
-Conference Call and Webcast to be Held at 8:30 a.m. ET Today-

SOUTH SAN FRANCISCO, Calif., Nov. 16, 2020 (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 positive initial clinical data from its ongoing Phase 1/2 trial for FLX475 in multiple cancer indications.

Initial observations as of November 10, 2020 from the ongoing trial for FLX475 include preliminary:

- evidence of monotherapy activity,
- encouraging efficacy in combination with the PD-1 checkpoint inhibitor pembrolizumab (marketed as Keytruda®) and
- biomarker data supporting FLX475's mechanism of action.

In addition, FLX475 demonstrated a favorable safety profile, both as monotherapy and in combination with pembrolizumab.

"We are pleased with the early evidence of clinical activity of FLX475, both as monotherapy and in combination with pembrolizumab in multiple charged tumor types," said Brian Wong, M.D., Ph.D., President and CEO of RAPT. "Based on these encouraging data, we have determined that three cancer indications, EBV^+ lymphoma, nasopharyngeal cancer and head and neck cancer, have generated sufficient early evidence of efficacy to advance into expanded Phase 2 evaluation. We continue to enroll patients and generate data in this multi-cohort, multi-indication trial and look forward to providing updates on all remaining cohorts and additional go-forward decisions next year."

Scott Antonia, M.D., PhD., Professor of Medicine and Director of the Duke Cancer Institute Center for Cancer Immunotherapy and a member of RAPT's Scientific Advisory Board, added, "FLX475 is a potent non-depleting CCR4 antagonist that is designed to block regulatory T cells that interfere with an effective anti-tumor immune response. These data are particularly impressive as the immunotherapy field has long recognized T_{reg} as important targets in oncology, but until FLX475, others have not been able to selectively target these cells in the tumor microenvironment without affecting beneficial cells. These data demonstrate that RAPT's oral small molecule approach with FLX475 holds promise in treating a variety of charged cancers."

Charged cancers are tumors that contain high levels of both regulatory T cells (T_{reg}) and CD8 T cells and express high levels of the ligands for CCR4.

Phase 1/2 Clinical Trial Design
The ongoing open-label Phase 1/2 study is enrolling patients with multiple types of cancer at leading cancer centers across the United States, Australia and Asia. The Phase 1 portion of the trial is focused on evaluating the safety, pharmacokinetics and pharmacodynamics of FLX475 as a monotherapy and in combination with pembrolizumab. The Phase 2 portion is designed to evaluate the degree of antitumor activity of FLX475 as a monotherapy and in combination with pembrolizumab specifically in patients with several types of charged tumors. Changes in the tumor microenvironment and other biomarkers are being evaluated in both phases of the study. For more information please visit clinicaltrials.gov identifier NCT03674567.

Phase 1 Dose Escalation Data
The dose escalation Phase 1 portion of the trial enrolled a total of 37 patients with cancers of different types. Nineteen patients were treated with one of four doses (25 mg, 50 mg, 75 mg or 100 mg once daily) of FLX475 monotherapy and 18 were treated with one of three doses (50 mg, 75 mg or 100 mg once daily) of FLX475 in combination with the standard dose of pembrolizumab. Disease control, defined as a best response of stable disease (SD), an unconfirmed or confirmed partial response (PR) or complete response (CR), was observed in 14 of the 17 evaluable monotherapy patients, including an unconfirmed partial response in a patient with relapsed metastatic cervical cancer. In the combination cohorts, disease control was observed in 13 of the 14 evaluable patients. This includes two confirmed partial responses: a patient with NSCLC who had progressed on prior checkpoint treatment (atezolizumab) and who remains on study after 18 months of treatment, and a patient with checkpoint inhibitor-naïve urothelial cancer who was on study for over nine months of treatment. In addition, preliminary data show an increase in the CD8 to T_{reg} ratio after treatment, which is consistent with the hypothesis that a CCR4 antagonist can block the recruitment of tumor T_{reg}, increase the CD8 to T_{reg} ratio and potentially enhance antitumor immunity.

The Phase 1 results also show FLX475 had a favorable safety profile, with no maximum tolerated dose reached. Two dose-limiting toxicities (DLTs) of asymptomatic QTc prolongation were observed in the monotherapy cohorts, one in the 75 mg cohort and one in the 100 mg cohort. No DLTs were observed in the Phase 1 combination cohorts. Based on the Phase 1 data, 100 mg was selected as the recommended Phase 2 dose for both the

monotherapy and combination therapy cohorts.

Phase 2 Data
The ongoing Phase 2 portion of the trial is enrolling a minimum of 80 patients with several types of charged tumors, 10 in each of eight cohorts, with four cohorts evaluating FLX475 as a monotherapy and four cohorts evaluating FLX475 in combination with pembrolizumab. The charged cancers include Epstein-Barr Virus (EBV)- or Human Papillomavirus (HPV)-associated cancers such as nasopharyngeal cancer, cervical cancer, and subsets of Hodgkin and non-Hodgkin lymphomas as well as head and neck cancer. Other charged tumor types include non-small cell lung cancer and triple-negative breast cancer. The protocol calls for expansion of cohorts to generate additional data based on promising clinical activity.

Based on the promising early results from the Phase 1/2 trial with FLX475 observed to date, RAPT has selected three cancer indications for expansion:

- *EBV$^+$ lymphoma* – Early data from the first two patients with EBV$^+$ lymphoma treated with FLX475 monotherapy show significant target tumor reduction, including one patient (1/2) who achieved a durable complete metabolic response and continues on study after more than nine months. RAPT plans to expand the EBV$^+$ lymphoma monotherapy cohort and initiate a separate expansion cohort in EBV$^+$ lymphoma in combination with pembrolizumab.
- *Checkpoint inhibitor-naïve nasopharyngeal cancer (NPC)* – Of the 10 evaluable patients with NPC treated with FLX475 monotherapy, seven of 10 (7/10) patients exhibited stable disease as best response. Seven of the 10 patients crossed over to combination therapy where significant clinical activity has been observed. Of the six evaluable patients who crossed over, five were checkpoint inhibitor naïve. All five (5/5) of the checkpoint inhibitor-naïve patients demonstrated significant tumor shrinkage, with three (3/5) of these patients showing a partial response (two confirmed and one unconfirmed). Based on these results, RAPT plans to open a combination cohort in checkpoint inhibitor-naïve NPC.
- *Checkpoint inhibitor-naïve head and neck cancer* – Of the 10 evaluable patients with head and neck cancers treated with FLX475 monotherapy, five of 10 (5/10) patients exhibited stable disease as best response. Six patients initially treated with monotherapy crossed over to combination therapy, with one achieving a partial response and a second patient with an unconfirmed partial response (2/6). Seventeen patients are enrolled in a separate combination treatment cohort, of which 10 are evaluable so far. Substantial tumor reduction has been observed in four of the 10 (4/10), including one confirmed complete response and three patients with greater than 20 percent tumor reduction. Based on these results, RAPT plans to expand the combination cohort in checkpoint inhibitor-naïve head and neck cancers.

In these Phase 2 cohorts, FLX475 demonstrated a favorable safety profile with once-daily oral dosing both as monotherapy and in combination with pembrolizumab.

Phase 2 Stage 1 Cohorts[a]	Evaluable (N)	ORR *(%)*[b]	DCR *(%)*[c]
EBV$^+$ lymphoma monotherapy	2	50%	50%
Nasopharyngeal monotherapy	10	-	70%
Nasopharyngeal (CPI-naïve) crossover	5	60%	100%
Head and Neck (CPI-naïve) monotherapy	10	-	50%
Head and Neck (CPI-naïve) crossover	6	33%	66%
Head and Neck (CPI-naïve) combination	10	10%	60%

[a] Interim data as of November 10, 2020 from the ongoing FLX475-02 Phase 1/2 study; data subject to change.
[b]ORR = objective response rate defined as unconfirmed and confirmed PR or CR
[c]DCR = disease control rate defined as unconfirmed and confirmed PR or CR and SD as best response

Conference Call Information
The Company will host a webcast conference call accompanied by a slide presentation to discuss initial data from the Phase 1/2 study of FLX475 today at 8:30 a.m. Eastern Time. The call can be accessed by dialing (833) 672-0665 (domestic) or (929) 517-0344 (international) and refer to conference ID 6772479. The webcast will be available for replay for two weeks.

About FLX475
FLX475 is a small molecule CCR4 antagonist designed to block the migration of regulatory T cells (T_{reg}) specifically into tumors, but not healthy tissues. T_{reg} represent a dominant pathway for downregulating the immune response, generally correlate with poor clinical outcomes and may limit the effectiveness of currently available therapies such as checkpoint inhibitors. RAPT is developing FLX475 for the treatment of a broad range of "charged" tumors, which represent cancer types the Company believes are most likely to respond to FLX475, where a large quantity of T_{reg} cells are likely to be the cause of immune suppression within the tumor. FLX475 may restore naturally occurring antitumor immunity alone and may synergize with a variety of both conventional and immune-based therapies, such as radiation, chemotherapy, checkpoint inhibitors, immune stimulators, cancer vaccines and adoptive T cell therapy.

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, including hematopoietic progenitor kinase 1 (HPK1) and general control nonderepressible 2 (GCN2), 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 clinical development progress, the significance of early results from Phase 1/2 clinical trials of FLX475 and plans with respect to Phase 2 expansions. 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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