RAPT Therapeutics Announces Publication of Phase 1a/1b Clinical Trial of Zelnecirnon (RPT193) to Treat Atopic Dermatitis in Allergy

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- *Positive clinical and molecular effects observed, with improvements demonstrated in key exploratory efficacy endpoints - percent change in EASI, EASI-50, vIGA and pruritis NRS - at four weeks*
- *Further deepening of response in percent change in EASI, EASI-50 and vIGA observed two weeks after end of treatment*
- *Significant changes in transcriptional profile of patients treated with zelnecirnon at Day 29, which were also significantly correlated with improvements in clinical efficacy measures*
- *Zelnecirnon was well tolerated with no serious adverse events*

SOUTH SAN FRANCISCO, Calif., Nov. 27, 2023 (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 inflammatory diseases and oncology, today announced that results from its previously disclosed Phase 1a/1b clinical trial of zelnecirnon (formerly RPT193) were published in *Allergy*. The Phase 1a portion of the trial was a standard single and multiple dose-escalation study in 72 healthy volunteers. The Phase 1b portion of the trial was a randomized, double-blind, placebo-controlled study examining zelnecirnon as monotherapy in 31 patients with moderate-to-severe atopic dermatitis (AD).

The findings showed that once-daily zelnecirnon treatment was generally well tolerated, with no serious adverse events reported, and all reported treatment-emergent adverse events were mild-to-moderate in nature across both patients with atopic dermatitis and healthy volunteers.

In the Phase 1b trial, after four weeks of treatment, patients with moderate-to-severe AD who received zelnecirnon showed a 36.3% change from baseline in the Eczema Area and Severity Index (EASI) score, a standard measure of disease severity, compared to 17.0% in the placebo group. Notably, in the two-week period following the end of treatment, the zelnecirnon group showed continued deepening of the response and a statistically significant difference compared to placebo with a 53.2% change from baseline in EASI at the six-week time point compared to 9.6% in the placebo group ($p < .05$). Further, significant changes in the transcriptional profile were seen in skin biopsies of zelnecirnon-treated versus placebo-treated subjects at Day 29, which were also significantly correlated with clinical efficacy measures.

The deepening of the response may be related to zelnecirnon's mechanism of action, which is upstream of other agents targeting cytokines or signaling pathways.

"We are pleased to have these exciting data published in the prestigious, peer-reviewed journal *Allergy*," said Brian Wong, M.D., Ph.D., President and CEO of RAPT Therapeutics. "These data strongly support the potential of zelnecirnon as a safe, once-daily, oral treatment for patients with atopic dermatitis which could be an attractive therapeutic alternative ahead of injectable drugs. We look forward to reporting top-line data from our Phase 2b trial in atopic dermatitis in mid-2024 and continuing to progress enrollment in our Phase 2a trial in asthma."

Key Findings from the Phase 1b Study in Patients with Atopic Dermatitis
In the Phase 1b study, 21 patients with moderate-to-severe atopic dermatitis were treated with 400 mg of zelnecirnon, administered orally once a day for four weeks, while 10 patients received placebo. The zelnecirnon group showed clear improvement in key efficacy measures compared to placebo at the end of the four-week treatment period, including percent change from baseline in the Eczema Area and Severity Index (EASI) score, validated Investigator Global Assessment (vIGA) and pruritis Numerical Rating Scale (NRS):

- Patients treated with zelnecirnon achieved a 36.3% change from baseline in EASI score compared with 17.0% in patients in the placebo group
- 42.9% of patients treated with zelnecirnon achieved a 50% change from baseline in EASI score (EASI-50) compared with 10.0% in the placebo group
- 4.8% of patients treated with zelnecirnon achieved a vIGA score of 0/1 and at least a two-point improvement over baseline compared with 0.0% in the placebo group; and
- 45.0% of patients treated with zelnecirnon achieved at least a four-point reduction in the pruritus NRS score, compared with 22.2% in the placebo group

Patients were also evaluated for exploratory endpoints at six weeks (two weeks after the end of treatment). At six weeks, the patients treated with zelnecirnon showed further deepening of the response in EASI score and vIGA:

- Patients treated with zelnecirnon achieved a 53.2% change from baseline in EASI score compared with 9.6% in patients in the placebo group
- 61.9% of patients treated with zelnecirnon achieved EASI-50 compared with 20.0% in the placebo group; and
- 14.3% of patients treated with zelnecirnon achieved a vIGA score of 0/1 and at least a two-point improvement over baseline compared with 0.0% in the placebo group

Based on exploratory statistical analyses, the difference between zelnecirnon and placebo on the percent change in EASI score and EASI-50 was statistically significant at Day 43 ($p < 0.05$). No other endpoints or timepoints achieved statistical significance.

Zelnecirnon was well tolerated in the Phase 1b study. No serious adverse events were reported, and all adverse events reported were mild or moderate in intensity. The overall safety profile of zelnecirnon in the Phase 1b study and from the Phase 1a study in healthy volunteers, suggests zelnecirnon is a well-tolerated oral drug that would not require any laboratory safety monitoring.

Based on the efficacy and safety data observed in the Phase 1b study, RAPT initiated a dose-ranging Phase 2b study in patients with moderate-to-severe AD and a Phase 2a study in asthma.

About the Phase 1a/1b Study of RPT193
The Phase 1a portion of the Phase 1a/1b trial was a standard single and multiple dose-escalation study in healthy volunteers. The data from the Phase 1a study demonstrated pharmacokinetics and pharmacodynamics that support once-daily oral dosing with zelnecirnon, and blinded safety data supported initiation of the Phase 1b portion of the trial.

The Phase 1b portion of the trial was a randomized, double-blind, placebo-controlled study of zelnecirnon as monotherapy in patients with moderate-to-severe AD. The study was conducted at multiple sites in the United States and enrolled 31 patients with moderate-to-severe AD who had an inadequate response to, or were intolerant of, topical corticosteroids. The primary endpoint of the Phase 1b study was safety. Secondary and exploratory endpoints include pharmacokinetics, biomarkers and clinical efficacy as evaluated by multiple measurements, including percent change in the Eczema Area and Severity Index (EASI) score, the validated Investigator Global Assessment (vIGA) and pruritis Numerical Rating Scale (NRS). The Phase 1b trial was not powered to achieve statistical significance for any particular endpoint.

About Zelnecirnon
Zelnecirnon is a small molecule oral therapy in development for the treatment of atopic dermatitis and other inflammatory diseases. Zelnecirnon is designed to selectively inhibit the migration of Th2 cells into inflamed tissues by blocking CCR4, a receptor highly expressed on Th2 cells. Preliminary data suggest that zelnecirnon also has the potential to modulate Th2 cell function by lowering the secretion of Th2 cytokines upon stimulation. In allergic inflammatory diseases such as AD, chemokines recruit Th2 cells via CCR4 into inflamed tissues, where the Th2 cells secrete proteins known to drive the inflammatory response. The role of Th2 cells has been clinically validated by injectable biologics targeting this pathway. Patients with atopic dermatitis express higher levels of CCR4 ligands compared with healthy humans; these ligands also correlate with the severity of disease. RAPT believes that by inhibiting CCR4, zelnecirnon has the potential to bring therapeutic benefit to patients across a broad spectrum of inflammatory diseases, including atopic dermatitis, asthma, chronic spontaneous urticaria, alopecia areata, prurigo nodularis, chronic rhinosinusitis with nasal polyps, allergic rhinitis and eosinophilic esophagitis.

About Atopic Dermatitis
Atopic dermatitis is a chronic, inflammatory skin disease characterized by skin barrier disruption and immune dysregulation. Patients with AD have chronically inflamed skin lesions that can cause debilitating pruritus (itch), which can severely impair quality of life. While there is a marketed injectable product for the treatment of AD, RAPT believes zelnecirnon, if approved, could fill an unmet medical need for the treatment of inflammatory disorders with the convenience of once-daily oral dosing.

About RAPT Therapeutics, Inc.
RAPT Therapeutics is a clinical-stage, immunology-based therapeutics company focused on discovering, developing and commercializing oral small molecule therapies for patients with significant unmet needs in inflammatory diseases and oncology. 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, zelnecirnon (RPT193) and tivumecirnon (FLX475), each targeting C-C motif chemokine receptor 4 (CCR4), for the treatment of inflammation and cancer, 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 within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as “anticipate,” “expect,” "look forward," “potential,” “plan,” “target” and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify 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 therapeutic potential of RAPT’s product candidates, clinical development progress and the timing of initiation, enrollment and completion of, and availability of results from, clinical trials of zelnecirnon (RPT193) and other statements that are not historical fact. Many factors may cause differences between current expectations and actual results, including unexpected or unfavorable safety or efficacy data observed during clinical studies, preliminary data and trends that may not be predictive of future data or results or that may not demonstrate safety or efficacy or lead to regulatory approval, clinical trial site activation or enrollment rates that are lower than expected, including

lower than expected enrollment in our Phase 2b clinical trial of zelnecirnon in AD, unanticipated or greater than anticipated impacts or delays due to macroeconomic conditions (including the long-term impacts of ongoing overseas conflicts, inflation, higher interest rates and other economic uncertainty), changes in expected or existing competition, changes in the regulatory environment, the uncertainties and timing of the regulatory approval process and the sufficiency of RAPT's cash resources. 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 filed with the Securities and Exchange Commission on November 13, 2023 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, except as required by law.

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