Rain Therapeutics Provides Interim Analysis of Phase 2 Basket Trial of Milademetan for MDM2-Amplified Advanced Solid Tumors (MANTRA-2)

- Two patients exhibited an unconfirmed partial response at their first scan, and two additional patients saw promising tumor regression activity out of ten efficacy evaluable patients, demonstrating monotherapy activity of milademetan in MDM2-amplified patients -

- Drug safety profile of milademetan preliminarily consistent with prior Phase 1 trial -

- Protocol amendment planned to adjust MDM2 copy number (CN) threshold to CN ≥8 from CN ≥12; MANTRA-2 continues to enroll -

NEWARK, Calif., November 4, 2022 (GLOBE NEWSWIRE) -- Rain Therapeutics Inc. (NasdaqGS: RAIN), (Rain), a late-stage biotechnology company developing precision oncology therapeutics with a lead clinical candidate, milademetan, an oral, small molecule inhibitor of the MDM2-p53 complex that reactivates p53, today announced preliminary data in the multicenter, single arm, open-label, Phase 2 basket trial evaluating milademetan, an oral mouse double minute 2 (MDM2) inhibitor, for the treatment of MDM2-amplified advanced solid tumors.

"We are encouraged by the preliminary observations from the MANTRA-2 trial," said Avanish Vellanki, co-founder and chief executive officer of Rain. "Treatment with milademetan led to tumor regression in patients previously treated with a multitude of therapies across a range of cancers. We look forward to expanding this dataset as the trial continues to enroll."

Dr. Richard Bryce, MBChB, chief medical officer of Rain continued, "In the first ten evaluable patients, we have observed activity with two unconfirmed partial responses (PRs) at their first scan and promising tumor regression activity in two patients following milademetan monotherapy. In addition, anti-tumor activity was observed in patients with genetic co-alterations, and in tumors with MDM2 copy number above 8. Hence, we plan to revise the protocol to include patients tested locally for MDM2 copy number of 8 and greater. We are encouraged by these preliminary data and we look forward to continuing the trial and evaluating additional data as they become available in the coming months."

The MANTRA-2 trial is designed to evaluate the safety and efficacy of milademetan monotherapy in patients with advanced or metastatic solid tumors refractory or intolerant to standard-of-care therapy and that exhibit wild-type p53 and a prespecified minimum MDM2 gene copy number. Approximately 65 patients are anticipated to be enrolled to receive milademetan. As of the latest data cutoff on October 26, 2022, 17 patients have been enrolled. The primary endpoint of the trial is objective response rate as measured by RECIST criteria. Secondary endpoints include duration of response, disease control rate progression-free survival by investigator assessment, overall survival and growth modulation index.

Preliminary Interim Data

- As of the latest data cutoff on October 26, 2022, 17 patients have been enrolled, 15 of whom have been dosed with milademetan
- Ten patients were efficacy-evaluable with CN ≥8 by central testing
    - A diverse set of tumor histologies were enrolled amongst the evaluable patients

    - Most tumors had co-alterations in oncogenes or tumor suppressors, including KRAS, EGFR, and PIK3CA amongst others
- Two unconfirmed PRs were observed with tumor regression of 34% and 30% (pancreatic and lung cancer, respectively)
    - The patient with pancreatic cancer is pending response confirmation and ongoing treatment
    - The patient with lung cancer is deceased due to COVID-19
- Two patients exhibited promising activity with tumor regression of 29% and 27% (biliary tract and breast cancer, respectively) and the patients are continuing with the investigational therapy
- Observed anti-tumor effect of milademetan in heavily pretreated, refractory patients, with a median of four prior therapies
- Safety profile to date is preliminarily consistent with prior Phase 1 trial of milademetan

Our updated corporate presentation includes details of the preliminary interim data for MANTRA-2 and is available on the "Corporate Presentation" section of the Rain website.

About Milademetan

Milademetan (also known as RAIN-32) is an oral small molecule inhibitor of the MDM2-p53 complex that reactivates p53. Milademetan has demonstrated antitumor activity in an MDM2-amplified subtype of liposarcoma (LPS) and other solid tumors in a Phase 1 clinical trial, supported by a rationally designed dosing schedule to mitigate safety concerns and widen the potential therapeutic window of MDM2 inhibition. Rain has completed enrollment in a Phase 3 trial of milademetan (MANTRA) in patients with LPS, and is evaluating milademetan in a Phase 2 tumor-agnostic basket trial in certain solid tumors (MANTRA-2). Rain anticipates commencing a Phase 1/2 clinical trial to evaluate the safety, tolerability and efficacy of milademetan in combination with Roche's atezolizumab in patients with loss of cyclin-dependent kinase inhibitor 2A (CDKN2A) and wildtype p53 advanced solid tumors (MANTRA-4), in the first quarter of 2023. Milademetan has received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for the treatment of LPS.

About Rain Therapeutics Inc.

Rain Therapeutics Inc. is a late-stage precision oncology company developing therapies that target oncogenic drivers to genetically select patients it believes will most likely benefit. This approach includes using a tumor-agnostic strategy to select patients based on their tumors' underlying genetics rather than histology. Rain's lead product candidate, milademetan, is a small molecule, oral inhibitor of MDM2-p53 complex that reactivates p53. In addition to milademetan, Rain is also developing a preclinical program that is focused on inducing synthetic lethality in cancer cells by inhibiting RAD52.

Forward Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include statements regarding, among other things, Rain's ongoing and planned trials for milademetan, including continued patient enrollment in MANTRA-2, the efficacy and safety of milademetan for the treatment of MDM2-amplified advanced solid tumors; timing for efficacy evaluable data in MANTRA-2 trial, expected trial design and the relationship between the results from the interim data from MANTRA-2 trial and results of future or ongoing clinical studies. Because such

statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as “plans,” “will”, “anticipates,” “goal,” “potential,” “expects” and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Rain’s current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks and uncertainties associated with Rain’s business in general and limited operating history, Rain’s ability to execute on its strategy, Rain’s reliance on third parties to conduct and support its preclinical studies and clinical trials, positive results from a clinical trial, or interim data from an ongoing clinical trial, may not necessarily be predictive of the results of future or ongoing clinical studies, the effect of the COVID-19 pandemic on Rain’s clinical trials and business operations, the impact of general economic, health, industrial or political conditions in the United States or internationally, additional state and federal healthcare reform measures that could result in reduced demand for Rain’s product candidates, the sufficiency of Rain’s capital resources and its ability to raise additional capital, and the other risks described in Rain’s Annual Report on Form 10-K for the year ended December 31, 2021 and subsequent filings with the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made and are based on management’s assumptions and estimates as of such date. Rain undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

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