Phase 1 Clinical Data of Milademetan Published in Journal of Clinical Oncology

– Intermittent dosing of milademetan, an inhibitor of the p53-MDM2 complex, potentially exhibits an avenue to address historical issues with cytopenias with this class of compounds–

– Phase 1 data in advanced dedifferentiated liposarcoma provides foundation for the registrational Phase 3 MANTRA trial –

NEWARK, Calif., January 23, 2023 (GLOBE NEWSWIRE) -- Rain Oncology Inc. (NasdaqGS: RAIN), ("Rain"), a late-stage company developing precision oncology therapeutics with its lead product candidate, milademetan, an oral, small molecule inhibitor of the p53-MDM2 complex that reactivates p53, today announced the publication of a peer-reviewed article titled, "A First-in-Human Phase I Study of Milademetan, an MDM2 Inhibitor, in Patients with Advanced Liposarcoma, Solid Tumors or Lymphomas" in the *Journal of Clinical Oncology*. Phase 1 clinical data in the paper highlight the activity and tolerability using intermittent dosing of milademetan across a range of tumor types including dedifferentiated liposarcoma (DD LPS), which represented the largest proportion of patients enrolled in the study (n=53).

"An intermittent dosing schedule (260 mg qd, 3/14 days) of our highly selective inhibitor of the p53-MDM2 complex, milademetan, resulted in favorable safety and clinical activity in the Phase 1 trial in DD LPS patients," said Robert Doebele, MD, Ph.D., co-founder, president and chief scientific officer of Rain. "We view the prior data leveraging the intermittent dosing schedule as potentially offering a compelling risk/reward benefit, laying the foundation for our registrational Phase 3 MANTRA trial."

"Historical challenges with MDM2 inhibition identified cytopenias as a concern, for which intermittent dosing may provide a solution," said Richard Bryce, MBChB, Rain's chief medical officer. "The intermittent dosing schedule identified may provide for a more favorable tolerability profile that we would expect to translate across a multitude of future therapeutic indications."

Key Article Highlights Include:

- All liposarcoma patients enrolled in the Phase 1 trial exhibited the DD LPS subtype
- Among DD LPS patients in the Phase 1 trial, median progression-free survival (mPFS) outcomes were maintained with intermittent dosing schedules (once daily [qd] on days 1-3 and 15-17 every 28 days; eg, 3/14 days) compared with extended (qd on days 1-21) / continuous (qd on days 1-28) schedules:
    - mPFS of patients across all doses/schedules (n=53): 7.2 months
    - mPFS of patients with 260 mg qd 3/14 intermittent schedule (n=16): 7.4 months
    - mPFS of previously treated patients with 260 mg qd 3/14 intermittent schedule (n=11): 8.0 months
    - mPFS of treatment-naïve patients in all doses/schedules (n=17): 14.6 months

- Although all tested DD LPS patients had MDM2 gene amplification (n=22), mPFS in DD LPS patients did not differ by levels of key biomarkers including *MDM2* or *CDK4* copy number or by mRNA expression levels of *MDM2*, *CDK4*, or *MDM4*.
- The preferred intermittent dosing schedule of milademetan (260 mg qd 3/14 days) mitigates dose-limiting hematologic adverse events while maintaining activity, leading to:
    - Marked reductions in occurrence and severity of grade 3/4 drug-related thrombocytopenia (15.8%; n=38) compared to extended/continuous schedules (36.2%; n=69) and
    - Fewer dose reductions (21.1%; n=8) and dose interruptions (15.8%; n=6) compared with extended/continuous schedules (23.3%; n=16 and 34.8%; n=24, respectively).
- Preliminary single-agent activity with milademetan in DD LPS prompted the ongoing, randomized Phase 3 MANTRA trial (NCT04979442), with topline data anticipated in the first quarter of 2023.

About Milademetan

Milademetan (also known as RAIN-32) is an oral small molecule inhibitor of the p53-MDM2 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 inhibition of the p53-MDM2 complex. 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 Oncology Inc.

Rain Oncology 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 the p53-MDM2 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, patient enrollment, timing for topline and interim data, including anticipated timing for topline data in the Phase 3 MANTRA trial, timing for the commencement of planned trials, and expected trial designs. 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 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, 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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