# PMV Pharmaceuticals Provides a Progress Update on PYNNACLE Clinical Trial

October 23, 2024

- *Enrollment on track in registrational Phase 2 portion of PYNNACLE clinical trial evaluating rezatapopt as monotherapy in patients with TP53 Y220C and KRAS wild-type advanced solid tumors; more than 75% of sites activated across the U.S., Europe, and Asia-Pacific; interim analysis expected by mid-2025*
- *Dose-limiting toxicities observed in rezatapopt and Merck's anti-PD-1 therapy KEYTRUDA (pembrolizumab) combination arm of Phase 1b PYNNACLE trial; rezatapopt 500 mg once-daily in combination with pembrolizumab 200 mg every three weeks established as maximum tolerated dose; due to limited clinical benefit at this dose, PMV is discontinuing enrollment in the Phase 1b combination arm*
- *PMV Pharmaceuticals is collaborating with MD Anderson Cancer Center (MDACC) and Memorial Sloan Kettering Cancer Center (MSK) to support an investigator-initiated Phase 1b study evaluating rezatapopt monotherapy and in combination with azacitidine in patients with recurrent or refractory AML/MDS harboring a TP53 Y220C mutation*

PRINCETON, N.J., Oct. 23, 2024 (GLOBE NEWSWIRE) -- PMV Pharmaceuticals, Inc. (Nasdaq: PMVP), a precision oncology company pioneering the discovery and development of small molecule, tumor-agnostic therapies targeting p53, today provided an update on the Phase 2 monotherapy and Phase 1b combination portions of the ongoing PYNNACLE clinical trial.

**PYNNACLE Phase 2 Monotherapy Update**

Enrollment is on track in the Phase 2 monotherapy portion of the PYNNACLE clinical trial. The multicenter, single-arm, registrational, tumor-agnostic Phase 2 trial is assessing rezatapopt as monotherapy at a dose of 2000 mg once-daily in patients with *TP53* Y220C and *KRAS* wild-type advanced solid tumors. The primary endpoint of the trial is overall response rate per blinded independent central review. The trial is designed to enroll 114 patients across five cohorts at approximately 60 sites.

More than 75% of sites have been activated across the U.S., Europe, and Asia-Pacific. PMV plans to provide data from the interim analysis of the Phase 2 monotherapy portion of the PYNNACLE trial by mid-2025 and anticipates submitting a New Drug Application by the end of 2026.

**PYNNACLE Phase 1b Rezatapopt in Combination with Pembrolizumab Update**

PMV has decided to discontinue enrollment in the Phase 1b combination arm of the PYNNACLE trial evaluating rezatapopt in combination with Merck's anti-PD-1 therapy KEYTRUDA (pembrolizumab) in patients with advanced solid tumors harboring a *TP53 Y220C* mutation. Nineteen patients were enrolled in the combination arm of the trial. This decision was driven by dose-limiting toxicities (DLTs) observed at the 1000 mg dose of rezatapopt once-daily plus pembrolizumab 200 mg every three weeks. The DLTs were Grade 2 and 3 and included AST increase, platelet count decrease, pancreatitis, dehydration, and rash. No Grade 4 or 5 adverse events were observed. The safety profile of the rezatapopt and pembrolizumab combination has been consistent with each agent as monotherapy with no new safety signals observed.

Per protocol, these observations established rezatapopt 500 mg once-daily in combination with pembrolizumab 200 mg every three weeks as the maximum tolerated dose. Patients dosed with rezatapopt 500 mg once-daily in combination with pembrolizumab did not experience a clinically meaningful benefit, informing the decision to discontinue enrollment in the combination arm of the PYNNACLE trial.

**MD Anderson Cancer Center and Memorial Sloan Kettering Cancer Center to Initiate a Phase 1b Study in Recurrent/Refractory AML/MDS**

PMV Pharma is collaborating with MD Anderson Cancer Center (MDACC) and Memorial Sloan Kettering Cancer Center (MSK) to support an investigator-initiated Phase 1b study. The study is designed to assess the safety, tolerability, pharmacokinetics, and preliminary efficacy of rezatapopt monotherapy and in combination with azacitidine in approximately 25 patients with recurrent or refractory acute myeloid leukemia (AML)/myelodysplastic syndromes (MDS) harboring a *TP53 Y220C* mutation. Enrollment is planned to begin in the first quarter of 2025 across two sites.

"There is an important need for new treatment options for patients with recurrent or refractory AML or MDS harboring a TP53 Y220C mutation, as this mutation is often associated with poorer prognosis and resistance to conventional therapies" said Courtney DiNardo M.D., MSCE, Department of Leukemia, Division of Cancer Medicine at MDACC. "Based on proof-of-concept data demonstrating the ability of rezatapopt to selectively reactivate p53 in locally advanced/metastatic solid tumor patients with a TP53 Y220C mutation, we believe that rezatapopt in combination with azacitidine has the potential to significantly benefit this patient population."

Eytan M. Stein, M.D., Chief, Leukemia Service at MSK commented, "Patients with p53 mutant AML currently have no effective standard of care treatment options that lead to long term survival, so this important trial using rezatapopt is the first step in developing a focused, mutation specific strategy, for this patient population."

David Mack, Ph.D., President and Chief Executive Officer of PMV Pharma commented, "While we are disappointed to discontinue enrollment of the trial evaluating rezatapopt in combination with pembrolizumab, we look forward to the initiation of the AML/MDS study and evaluating rezatapopt in other settings. I would like to thank the patients and investigators for their time and commitment to the Phase 1b combination portion of the PYNNACLE study. We remain excited by the potential for rezatapopt as a monotherapy in patients with advanced solid tumors harboring a TP53 Y220C mutation and KRAS wild-type and look forward to providing interim data in the middle of next year."

KEYTRUDA® (pembrolizumab) is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

**About Rezatapopt**

Rezatapopt (PC14586) is a first-in-class, small molecule p53 reactivator designed to selectively bind to the pocket in the p53 Y220C mutant protein, restoring the wild-type tumor-suppressor function. The U.S. Food and Drug Administration (FDA) granted Fast Track designation to rezatapopt for the treatment of patients with locally advanced or metastatic solid tumors with a TP53 Y220C mutation.

**About the PYNNACLE Clinical Trial**

The ongoing Phase 1/2 PYNNACLE clinical trial is evaluating rezatapopt in patients with advanced solid tumors harboring a TP53 Y220C mutation. The primary objective of the Phase 1 portion of the trial was to determine the maximum tolerated dose and recommended Phase 2 dose (RP2D) of rezatapopt when administered orally to patients. Safety, tolerability, pharmacokinetics, and effects on biomarkers were also assessed. In Phase 1, an overall response rate of 38% (6/16 evaluable patients) was achieved at the RP2D of 2000 mg daily reflective of the Phase 2 patient population (TP53 Y220C and KRAS wild-type). The median duration of response was seven months. The Phase 2 monotherapy portion is a registrational, single-arm, expansion basket clinical trial comprising five cohorts (ovarian, lung, breast, endometrial cancers, and other solid tumors) with the primary objective of evaluating the efficacy of rezatapopt at the RP2D in patients with TP53 Y220C and KRAS wild-type advanced solid tumors.

For more information about the Phase 1/2 PYNNACLE clinical trial, refer to www.clinicaltrials.gov (NCT trial identifier NCT04585750).

**About PMV Pharma**

PMV Pharma is a precision oncology company pioneering the discovery and development of small molecule, tumor-agnostic therapies targeting p53. TP53 mutations are found in approximately half of all cancers. Our co-founder, Dr. Arnold Levine, established the field of p53 biology when he discovered the p53 protein in 1979. Bringing together leaders in the field to utilize over four decades of p53 biology, PMV Pharma combines unique biological understanding with a pharmaceutical development focus. PMV Pharma is headquartered in Princeton, New Jersey. For more information, please visit www.pmvpharma.com.

**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. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding our future plans or expectations for rezatapopt, including our ability to obtain approval as a treatment option on a tumor-agnostic basis and as a monotherapy or in combination with other agents, expectations regarding timing for interim data readouts and success of the Phase 2 portion of the PYNNACLE trial, our expectation and timing of NDA filing(s) with the FDA for the current clinical trial for rezatapopt, the current and future enrollment of patients in our clinical trials, the timing, progress and activation of sites for our clinical trials, and plans for MDACC and MSKCC’s investigator-initiated study assessing rezatapopt as monotherapy and in combination with azacitidine for treatment of recurrent or refractory AML/MDS patients. Any forward-looking statements in this statement are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include: the success, cost, and timing of our product candidate development activities and planned clinical trials, our ability to execute on our strategy and operate as a clinical stage company, the potential for clinical trials of rezatapopt or any future clinical trials of other product candidates to differ from preclinical, preliminary or expected results, our ability to fund operations, and the impact that a global pandemic, other public health emergencies or geopolitical tensions or conflicts may have on our clinical trials, supply chain, and operations, as well as those risks and uncertainties set forth in the section entitled “Risk Factors” in our Annual Report on Form 10-K, filed with the Securities and Exchange Commission (the “SEC”) on February 29, 2024, our Quarterly Report on Form 10-Q for the three months ended March 31, 2024, filed with the SEC on May 9, 2024, and our other filings filed with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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