Mural Oncology's First Virtual Investor Day to Highlight Late-Stage Clinical Progress

September 26, 2024

Key data readouts for the company's late-stage, potentially registrational trials of nemvaleukin are expected in late Q1/early Q2 2025 for platinum-resistant ovarian cancer and Q2 2025 for mucosal melanoma

Management team to provide additional information not previously disclosed related to nemvaleukin study design, statistical assumptions, and study execution

Clinicians to discuss treatment landscape of platinum-resistant ovarian cancer and mucosal melanoma, two indications with limited treatment options and poor outcomes for patients

IND submission for Mural's IL-18 program planned for Q4 2025

WALTHAM, Mass and DUBLIN, Sept. 26, 2024 (GLOBE NEWSWIRE) -- Mural Oncology plc (Nasdaq: MURA), a clinical-stage immuno-oncology company developing novel, investigational engineered cytokine therapies designed to address areas of unmet need for patients with a variety of cancers, will host a virtual Investor Day today beginning at 10 a.m. ET. Mural leadership will provide new clinical insight into the trial design, statistical assumptions, and progress of the company's late-stage trials of nemvaleukin.

"Mural has the most advanced IL-2 program currently in development and we have made significant progress this year. We have a great deal of conviction around nemvaleukin, which is engineered to unlock the efficacy potential of high dose IL-2 for more patients, and we are pleased to share more details around our study designs and assumptions during today's Investor Day," said Caroline Loew, Ph.D., CEO of Mural Oncology. "There has also been significant interest in our IL-18 program and we announced today that we plan to submit an IND to the FDA for this program in Q4 2025. Together we believe these programs have the potential to be the next wave of much needed treatment options for cancer patients."

ARTISTRY-7:
ARTISTRY-7 is a potentially registrational phase 3 trial comparing the combination of nemvaleukin and pembrolizumab versus investigator's choice single agent chemotherapy in heavily pre-treated patients with platinum-resistant ovarian cancer (PROC), with a primary endpoint of overall survival (OS). Secondary endpoints include progression free survival, overall response rate, disease control rate, duration of response, time to response, CA-125 response, and treatment emergent adverse events. This four-arm trial also contains two smaller monotherapy arms to assess contribution of components.

PROC is an area of high unmet need, with few effective treatment options and poor survival. Nemvaleukin for the treatment of PROC has received Food & Drug Administration (FDA) Fast Track Designation.

Enrollment is complete, with a total of 456 patients (versus 448 planned), and approximately 187 patients in each of the two experimental arms.

Futility analyses are complete for both monotherapy arms:
Pembrolizumab (arm 2):

- Predetermined analysis criteria were based on Keynote-100 trial, where single agent pembrolizumab was evaluated in 376 patients with PROC with a response rate of 8%.
- Futility in this arm of ARTISTRY-7 was defined as fewer than two confirmed complete or partial responses in the first 12 patients enrolled.
- This arm was closed to further enrollment for futility in August 2023 after enrolling 27 patients.

Nemvaleukin (arm 3):

- Predetermined futility criteria were based on two historical phase 2 trials using different doses and schedules of aldesleukin, an approved high-dose IL-2, that showed consistent response rates of approximately 25%, including some patients with durable complete responses.[1]
- Futility criteria for this nemvaleukin single arm required at least one patient among the first 24 enrolled to achieve an objective response or stable disease for at least three months to continue enrollment.
- The nemvaleukin single arm met this threshold to continue and ultimately enrolled 55 patients.

No statistical comparisons will be performed on the pembrolizumab and nemvaleukin monotherapy arms; all analyses of these two arms will be descriptive.

ARTISTRY-7 Overall Survival Expectations and Rationale
Based on benchmarking against prior phase 3 trials in PROC, which had different eligibility criteria regarding the number of prior therapies, and the eligibility criteria of ARTISTRY-7 which allow for up to five prior lines of therapy in the platinum-resistant or refractory setting, protocol assumptions are:

- A median Overall Survival (OS) of 10 months for the chemotherapy control arm.

- A median OS of 14.3 months for the nemvaleukin plus pembrolizumab experimental arm.

ARTISTRY-7 Events and Statistics:

- Protocol specific **interim analysis for OS** will occur at 75% of OS events (~215 of 286 total OS events).
- **Cumulative alpha spend** at interim analysis is 1-sided, 0.0096.
- **Maximum hazard ratio** for success at the interim analysis is 0.727 (a 27.3% reduction in the risk of death), assuming exactly 215 OS events.

ARTISTRY-7 Timing:

- With enrollment complete, the OS events required for interim analysis are estimated to occur by late Q4 2024 or early Q1 2025.
- Mural expects the interim analysis data readout to be available in late Q1 or early Q2 2025.
- If the hazard ratio meets the bar for success, the study will be declared positive and the company will plan to file a Biologics License Application (BLA) in 2025.
- If the target hazard ratio is not met, the company may decide to continue to final analysis at approximately 286 OS events, or it may decide to terminate the study.

ARTISTRY-6, Cohort 2:
ARTISTRY-6 cohort 2 is a potentially registrational single arm study of single agent nemvaleukin in patients with unresectable or metastatic mucosal melanoma. The trial's primary endpoint is overall response rate evaluated per RECIST 1.1 by an independent central radiology review. Secondary endpoints include duration of response, time to response, disease control rate, progression-free survival, and safety.

Mucosal melanoma is a rare subtype of melanoma with poor prognosis and currently no approved treatment options. Nemvaleukin for the treatment of mucosal melanoma has received both FDA Fast Track Designation and Orphan Drug Designation.

Enrollment in this study is complete with 92 patients enrolled.

ARTISTRY-6, Cohort 2 Response Rate Assumptions and Rationale:
The target response rate is 25%. At this target, the lower bound of the 95% confidence interval will exceed a 15% response rate.

Mural believes that in this rare and highly aggressive tumor with poor outcomes even in the first line setting, demonstrating durable responses with a response rate of 20-25% would be meaningful for patients, and would support a discussion with the FDA regarding a potential BLA submission and potential accelerated approval.

A potential accelerated approval would require confirmatory evidence to be agreed with and later submitted to the FDA for conversion to a regular approval. Discussions with FDA on a potential confirmatory evidence package are ongoing.

ARTISTRY-6 Timing:

- The primary analysis will occur when all patients have a minimum follow-up of at least six months. In order to ensure adequate follow-up on all patients, Mural anticipates that the top-line readout will occur in the second quarter of 2025.
- Potential accelerated approval with confirmatory evidence to be later submitted for conversion to regular approval.
- Regulatory filing may be deferred if the ARTISTRY-7 study continues to final analysis, pending the final outcome.

Mural Oncology's IL-18 Program :

Mural plans to nominate a development candidate for its IL-18 program by the end of 2024 and intends to submit an Investigational New Drug (IND) Application to the FDA in Q4 2025.

Mural Investor Day Webcast Details:
Mural's management team will be joined by three clinicians on the webcast to discuss the treatment landscape for PROC and mucosal melanoma, as well as nemvaleukin's clinical proof of concept data.

The live webcast will begin at 10 a.m. followed by a Question & Answer session. To join the webcast, please visit https://ir.muraloncology.com/events-and-presentations.

A replay of the webcast will be available shortly after the conclusion of the meeting.

About Mural Oncology
Mural Oncology is leveraging its novel protein engineering platform to develop cytokine-based immunotherapies for the treatment of cancer. By combining our expertise in cytokine biology and immune cell modulation and our protein engineering platform, we are developing medicines to deliver meaningful and clinical benefits to people living with cancer. Our mission is to broaden the potential, and reach, of cytokine-based immunotherapies to improve the lives of patients. Our lead candidate, nemvaleukin, is currently in potentially registrational trials in mucosal melanoma and platinum-resistant ovarian cancer reading out in the first half of 2025. Mural Oncology has its registered office in Dublin, Ireland, and its primary facilities in Waltham, Mass. For more information, visit Mural Oncology's website at www.muraloncology.com and follow us on LinkedIn and X.

About Nemvaleukin
Nemvaleukin alfa (nemvaleukin) is a novel, engineered cytokine designed to leverage antitumor effects of the IL-2 pathway while mitigating the hallmark toxicities that limit its use. Nemvaleukin selectively binds to the intermediate-affinity IL-2 receptor (IL-2R) and is sterically occluded from binding to the high-affinity IL-2R. Because of this molecular design, nemvaleukin treatment leads to preferential expansion of antitumor CD8+ T cells and natural killer cells, with minimal expansion of immunosuppressive regulatory T cells. Nemvaleukin is currently being evaluated in two potentially registrational late-stage trials.

About Mural Oncology's IL-18 Program
IL-18 is a potent immune-stimulating cytokine, but its efficacy is blunted by IL-18 binding protein (IL-18BP), a high affinity decoy receptor that binds to, and neutralizes, IL-18, thereby rendering it ineffective. Native IL-18's potency is also limited by its short half-life. Mural Oncology's novel approach to

protein engineering is designed to mitigate these issues. First, Mural introduced mutations to IL-18 that eliminate binding to IL-18BP while minimally impacting the native IL-18 structure. Second, it fused IL-18 to protein scaffolds which extend the half-life and increase IL-18's exposure. Together, these have demonstrated more durable immunological effect in preclinical studies. Mural intends to nominate a development candidate for its IL-18 program by the end of this year and file an IND submission by the end of 2025.

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: the company's pipeline and development programs, including the expected timing of clinical updates from the ARTISTRY-6 and ARTISTRY-7 trials, the expected timing of preclinical updates, candidate nomination, and IND submission, including with respect to the Company's IL-18 program, the potential of the company's product candidates and programs to address unmet medical needs, and the continued progress of its pipeline and programs. Any forward-looking statements in this press release 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, among others, the inherent risks and uncertainties associated with competitive developments, preclinical development, clinical trials, recruitment of patients, product development activities and regulatory approval requirements; that preclinical or interim results and data from ongoing clinical studies of the company's cytokine programs and product candidates may not be predictive of future or final results from such studies, results of future clinical studies or real-world results; future clinical trials or future stages of ongoing clinical trials may not be initiated or completed on time or at all; the company's product candidates, including nemvaleukin, could be shown to be unsafe or ineffective; changes in the cost, scope and duration of development activities; the U.S. Food and Drug Administration may make adverse decisions regarding the company's product candidates; and those other risks and uncertainties set forth in the company's filings with the Securities and Exchange Commission ("SEC"), including its Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2024 and in subsequent filings the company may make with the SEC. All forward-looking statements contained in this press release speak only as of the date of this press release. The company anticipates that subsequent events and developments will cause its views to change. However, the company undertakes no obligation to update such forward-looking statements to reflect events that occur or circumstances that exist after the date of this press release, except as required by law.

Contact:
Katie Sullivan
katie.sullivan@muraloncology.com

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[1] Edwards et al. "Comparison of toxicity and survival following intraperitoneal recombinant interleukin-2 for persistent ovarian cancer after platinum: twenty-four-hour versus 7-day infusion." Journal of Clinical Oncology, November 1, 1997; Vlad et al. "A phase II trial of intraperitoneal interleukin-2 in patients with platinum-resistant or platinum-refractory ovarian cancer." Cancer Immunology and Immunotherapy, February 2010.