September 30, 2025

September 2025 Letter to Shareholders

VANCOUVER, Washington, Sept. 30, 2025 (GLOBE NEWSWIRE) --

Dear Shareholders,

As this pivotal year continues to take shape for CytoDyn Inc. (“CytoDyn” or the “Company”), I am pleased to share the progress we have made in advancing leronlimab as an innovative treatment in oncology. We remain confident that addressing critical unmet needs in this field is the best way to build value while improving the lives of patients. The foundation of our conviction in leronlimab rests on both preclinical and clinical evidence. From laboratory insights to encouraging patient survival observations, our story is compelling and one of consistent validation. The data presented over the past several months marks a watershed moment for both patients and our Company, providing evidence that leronlimab has the potential to reshape treatment paradigms in solid tumor oncology. With multiple clinical trials advancing, we are moving with discipline and urgency along a well-defined path forward.

Strengthening Our Leadership

To support this next chapter, we welcomed Robert E. Hoffman as our new Chief Financial Officer. An industry veteran with decades of financial and leadership experience, holding various executive and board positions in his biotech career, Robert has already brought significant value to CytoDyn. His expertise in capital markets and strategic planning strengthens our ability to execute, network, and expand our pipeline. We are delighted to have him aboard.

Scientific Progress and Clinical Development

At the heart of leronlimab’s promise is a novel mechanism of action (“MOA”) associated with prolonged survival observed in a group of patients with Metastatic Triple-Negative Breast Cancer (“mTNBC”). Supporting data, presented at a poster session at the European Society for Medical Oncology (“ESMO”) breast cancer meeting in Munich, suggest that leronlimab induces PD-L1 expression, creating synergy with immune checkpoint inhibitors (ICIs), a potential breakthrough in solid tumor treatment. This finding not only opens new therapeutic opportunities for leronlimab, but also represents a significant market opportunity for the Company. For additional information on this novel MOA and the status of our clinical initiatives and publications, please see the science update included with this letter.

One indication that carries the potential for significant value return is leronlimab in mTNBC, the most aggressive form of breast cancer, with 5-year survival rates around 15%. Based on the positive data presented at ESMO, we will shortly submit a follow-up Phase II proof of concept (POC) protocol for PD-L1-negative patients with mTNBC. These patients, currently ineligible for ICI therapy, will receive leronlimab plus standard chemotherapy, followed by a regimen of leronlimab with an ICI. We look forward to sharing more details after the FDA review of the protocol and briefing package that provides a complete summary of CytoDyn’s oncology data.

In parallel, we will be submitting an Expanded Access Protocol (“EAP”) to enable treatment for patients with second-line, or later, mTNBC, who are ineligible or otherwise unable to participate in our Phase II study. I am pleased to announce that we will be working with an individual benefactor to fund the launch of this compassionate-use program. This benefactor has also expressed interest in supporting an investigator-initiated study in patients with recurrent glioblastoma with an anticipated start date in 2026.

Beyond breast cancer, leronlimab continues to advance in the treatment of metastatic Colorectal Cancer (mCRC). Enrollment in our Phase II study is underway with five sites initiated and several more onboarding in the next several weeks. The enrollment of our fifth patient in the trial will trigger the Data Safety Monitoring Board (DSMB) safety review, which could then open study randomization to include the 700 mg dose. Importantly, we will be closely tracking PD-L1 levels of enrolled patients to further validate our MOA across solid tumors. With that in mind, we have prepared a rollover protocol to ensure that CRC patients who remain stable can continue leronlimab treatment beyond 48 weeks and to allow patients with disease progression the opportunity to receive leronlimab at a dose of 700 mg in combination with an ICI.

Finally, I am happy to share a very promising announcement as it relates to a patient who prospectively upregulated PD-L1 after having obtained access to leronlimab through an eIND application submitted by her treating physician. In early 2025, we received a compassionate access request for a patient with mTNBC who was previously unresponsive to treatment with Keytruda. This particular patient had two prior tissue biopsies, both of which were PD-L1 negative. In April, the patient started treatment with leronlimab, and in July blood tests confirmed an increase in PD-L1 levels. Our past clinical observations have shown that upregulating PD-L1 is the first step towards prolonged survival in this patient population and we are encouraged by this readout, which supports our working theory. This is the first of hopefully many PD-L1 upregulation readouts across our CRC and TNBC trial(s) in the coming year. I continue to have high hopes for our upcoming Phase II trials, as well as our expanded access program, as we look to reshape treatment paradigms in solid tumor oncology.

Update on Regulatory Matters, Resolution of SEC and DOJ Investigations

I am also pleased to share that we recently received confirmation from both the Securities and Exchange Commission (“SEC”) and Department of Justice (“DOJ”) that their respective investigations have now closed, and nothing further is required of the Company. I believe this positive conclusion for the Company is a reflection of our team here and our collective commitment to compliance and cooperation.

I remain confident that our collaborative relationship with the FDA has placed us on a productive trajectory. To accelerate progress in oncology, we established an oncology advisory board focused on pursuing the fastest and most responsible pathway(s) forward. The FDA recently granted our request for a meeting, and we look forward to discussing our retrospective data set and related observations in TNBC, as well as the next steps in our TNBC development plan. Maintaining strong relationships and credibility with the FDA and industry partners remains a top priority as we move forward.

Commitment to our Shareholders

Your support has carried the Company through the last several years and we remain committed to acting in your best interests. I want to thank you all again for your perseverance and patience. Your questions and feedback are always appreciated and best received through the Company's IR email account: ir@cytodyn.com. In the coming months, we will be engaging in critical conversations with our key opinion leaders, potential industry partners and regulators. In support of these efforts, we ask our shareholders to be mindful of the process and respectful of our counterparties. Excessive outreach to these third parties can inadvertently hinder our progress. Our recent results and the novel MOA have attracted the attention of numerous patients, treating physicians, and others across the industry. Please know that we are actively pursuing collaborations to maximize the potential of leronlimab.

A Human Reminder of Our Mission

In closing, I'd like to share a brief personal anecdote. As the Company has worked to confirm the mTNBC survival observations and arranged for related follow-up testing, I've had the opportunity to speak with several of the surviving patients who accessed leronlimab during the Company's prior oncology studies. These are individuals who had exhausted all other options yet are now enjoying more time with their families. I had the privilege of sharing a meal with one survivor and her spouse and it is difficult to put into words the emotions we all felt when reflecting on the remarkable sequence of events that brought us together that night, but I can name the most prominent – hope. Encounters like these remind us why our work matters and fuel our determination to accelerate progress for patients everywhere.

With Gratitude,

Jacob Lalezari, MD
CEO

Note Regarding Forward-Looking Statements

This news release contains forward-looking statements relating to, among other things, mechanism of action, clinical trial results, product development, market position, future operating and financial performance, and business strategy. The reader is cautioned not to rely on these statements, which are based on current expectations of future events. For important information about these statements and our Company, including the risks, uncertainties and other factors that could cause actual results to vary materially from the assumptions, expectations and projections expressed in any forward-looking statements, the reader should review our Annual Report on Form 10-K for the fiscal year ended May 31, 2025, including the section captioned "Forward-Looking Statements" and in Item 1A, and in subsequent reports filed with the Securities and Exchange Commission. CytoDyn Inc. does not undertake to update any forward-looking statement as a result of new information or future events or developments other than as required by law.

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Science Supplement

– **September 2025** –

History of leronlimab in mTNBC

Dr. Richard Pestell, our Lead Consultant – Preclinical and Clinical Oncology, has published preclinical data demonstrating that leronlimab both prevented the metastatic spread of TNBC and caused reversal of established metastases in mice. These important observations speak to two different mechanisms by which leronlimab's blockade of the CCR5 receptor appears to impact cancer: the first involves the **role that CCR5 plays in cell migration** and how that receptor is hijacked by cancer cells to promote the spread of distant metastases; the second speaks to the **direct anti-cancer activity of leronlimab on an established tumor itself** and, in particular, the surrounding microenvironment.

To follow up on these preclinical observations, CytoDyn conducted three clinical studies in patients with mTNBC and other solid tumors starting in 2019. Analysis of pooled follow-up data from the 28 patients with mTNBC enrolled across these studies formed the basis for our presentation at ESMO and provided evidence of leronlimab's stand-alone activity in three important ways:

1. **Promising survival rates:** Overall survival rates at years 1, 2, 3, and 4 (35.7%, 21.4%, 17.9%, and 17.9%) compare favorably with previous studies of patients with advanced mTNBC. In particular, the long-term survival rates of 17.9% at both years 3 and 4 are very exciting, considering other studies exploring potential mTNBC treatments typically don't even report survival rates out to three years. Moreover, the survival rate of 17.9% at year 4 was calculated without removing or "censoring" patients who dropped out for any reason, meaning it is presented in the most conservative way possible.

2. **Impact on advanced disease:** Patients in our study population had failed a median of two prior lines of treatment *after* developing metastatic disease, and a majority had cancer in other organs (64% had visceral metastases and 29% had brain metastases at entry into the studies). Despite that, the median overall survival ("mOS") of 6.8 months for all 28 patients (9.7 months for the 18 patients receiving > 525 mg) appears comparable to the current standard of care. This makes our results especially promising, given our study population had, generally speaking, more advanced disease than typical clinical populations. Given our survival observations and working theory on the mechanism of action, we are excited to explore leronlimab as an earlier line of therapy with the idea that earlier treatment could serve to save more lives.

3. **Decreased CTC levels:** The decline in circulating tumor cells ("CTCs") observed in most patients after as little as one dose of leronlimab was significantly associated with both progression-free and overall survival. Leronlimab's rapid and prognostically significant impact on CTCs, which appears to reflect activity within the primary tumor

itself, provides important evidence of leronlimab's activity as a stand-alone agent. Confirming the full extent of leronlimab's activity on the primary tumor is on our short list of clinical priorities in the coming months.

CytoDyn's Presentation at ESMO – Outlining a Novel Mechanism of Action

As announced leading up to the ESMO presentation, the survival observations and related retrospective data collectively suggest a potential paradigm shift in solid tumor oncology involving leronlimab's novel mechanism of action in conjunction with Immune Checkpoint Inhibitors ("ICIs"). To help understand this new paradigm, the following is an explanation of the basic steps and the Company's working theory at this time:

For a cancerous tumor to establish itself and grow in the body, it attempts to avoid detection and an immune response. One way a cancer can do this is by hijacking CCR5, a protein receptor on the surface of certain immune cells. Through CCR5 signaling, the tumor commandeers host macrophages, a type of white blood cell that would otherwise attack the cancer cells, to help the tumor build a surrounding area or "microenvironment" to support its growth, including a blood supply that provides necessary nutrients. The growing tumor also uses CCR5 signaling to recruit immunosuppressive cells to the local environment that keep the microenvironment "cold" and the host immune system at bay.

As to the above processes, it appears leronlimab has the ability to disrupt the CCR5 signaling that both promotes the cancer tumor's growth and protects its microenvironment from the host immune response. By disrupting CCR5 signaling, leronlimab allows the host immune system (CD8+ cells) to identify the cancer cells as a threat and attack them in what has now become a "hot" or inflamed microenvironment (expressing various inflammatory cytokines).

To counter the pressure of an attack from the host immune system, the cancer, at least as evidenced on the CTCs, has a secondary line of defense: expressing a protein called PD-L1 and hijacking its relationship to its receptor, PD-1. Ordinarily, PD-1 acts as the immune system's "off switch", binding with PD-L1 on functioning immune cells and preventing them from being so strong that they kill healthy cells in the body. Cancer cells capitalize on this system by expressing PD-L1 and binding to the "off switch" on the invading host immune cells, in turn slowing an immune response, thereby protecting the tumor.

As observed in patients who were fortunate enough to receive a PD-L1 antibody called an ICI in our prior studies, this "secondary defense" of the tumor can be thwarted. The antibody prevents the PD-L1 protein from binding to the "off switch" (PD-1), keeping the immune system "on" and allowing the host immune system's attack on the cancer to continue. Typically, patients who have tumors with higher levels of PD-L1 expression derive the most benefit from treatment with an ICI, given there are more opportunities for the antibody to block connections to the "off" switch and allow the immune system to fight the cancer cells.

As to this process, preliminary data indicate that leronlimab has the ability to induce higher levels of PD-L1 expression in solid tumor cancer cells. This opens potential new treatment pathways for patients with low PD-L1 levels who would have otherwise been unable to derive benefit from an ICI.

The foregoing sequence is a novel working theory; however, our data, first presented at

ESMO, suggest that this is what happened in the five patients who are alive today, 48 months after diagnosis.

The key findings from our presentation at ESMO included the following:

- **PD-L1 Upregulation**: 16/21 (76%) of patients showed a significant increase in PD-L1 expression on CTCs within 30-90 days after starting leronlimab, regardless of dose. This suggests that the tumor microenvironment was turned from "cold" to "hot" (from being protected against host immune invasion to being under host immune attack). Even more remarkably, this shift from "cold" to "hot" occurred in 15/17 (88%) patients who received weekly leronlimab doses of 525 mg or higher. Turning "cold" tumors "hot" means that far more patients with TNBC (and potentially other solid tumors) may become eligible for a class of drugs known as anti-PD-1/anti-PD-L1 treatments and collectively referred to as ICIs.

- **Long Term Survival**: The clinical significance of the increase in PD-L1 observed on the CTCs was driven home by the confirmation that 5/5 (100%) of patients who demonstrated a significant increase in PD-L1 expression while receiving leronlimab *and* received any ICI are alive today, 4+ years later. More remarkably, three of these individuals (60%) are currently identified as having no ongoing evidence of disease. Underscoring the clinical significance of these results is the unfortunate finding that none of the 23 patients who didn't induce significant PD-L1 expression or didn't receive an ICI with leronlimab are alive today.

Update(s) on Colorectal Cancer and Pending Trial

While generating the TNBC dataset, we documented outcomes in patients with other solid tumors previously enrolled in the CD09 "Basket Study." The results from five such patients with colorectal cancer ("CRC") were presented at the ESMO GI meeting in Barcelona this past July by the Principal Investigator for our current CRC study, Dr. Ben Weinberg from the Lombardi Comprehensive Cancer Center at Georgetown University. Additional updates on our CRC trial and how we will be using the CRC trial to further establish our working theory on the mechanism of action driving improved survival are included below.

The timing of the TNBC observations, data set, and working mechanism of action theory creates a unique opportunity for CytoDyn to evaluate this "cold to hot" paradigm shift in the context of a second solid tumor during our CRC study. Up to 85% of patients with CRC are not currently candidates for ICI therapy because their tumors are "cold" and do not express PD-L1. Our mCRC study design provides leronlimab in both arms of the study. As such, we have amended the protocol to include close monitoring of PD-L1 levels on the CTCs in all enrolled patients. In addition, we are submitting a new rollover protocol to the FDA, which will provide ongoing access to leronlimab for those patients with CRC who continue to do well after 48 weeks on the parent study and will now offer leronlimab plus an ICI to those patients who progress on the parent study. These amendments will allow us to achieve multiple critical goals, including:

- Evaluate leronlimab as a stand-alone agent (in combination with Standard of Care) in a second solid tumor type;
- Prospectively evaluate the ability of 2 different leronlimab dose levels to induce PD-L1 expression on CTCs in a solid tumor that is typically "cold" and not usually associated

with PD-L1 expression;
- Obtain biopsy tissue from patients with disease progression enrolling in the rollover protocol to correlate PD-L1 levels and changes in the tumor microenvironment on tumor tissue with PD-L1 expression on concurrently drawn CTCs; and
- Evaluate the possibility of treating patients with a common and typically “cold” cancer with the combination of leronlimab and an ICI, the same regimen that demonstrated long-lasting remission in 5/5 patients with mTNBC who significantly induced PD-L1, as reported at ESMO.

It is fortuitous that we launched the CRC study just as the PD-L1 data came to light, as it allows us to immediately commence efforts to collect certain prospective confirmatory data. Five trial sites have been initiated. It is our hope that the ESMO CRC data, together with the option of receiving leronlimab and an ICI during the rollover protocol, will generate interest among both patients and caregivers and help to expedite enrollment efforts.

Investigator-Initiated Study in Glioblastoma

In addition to mTNBC and CRC, we are continuing our investigation into a possible role for leronlimab in the treatment of glioblastoma, a third solid tumor type. We have found an individual who has agreed to fund this venture, and we have reached a tentative agreement with two medical centers to support their investigator-initiated pilot study in patients with recurrent glioblastoma. These patients will receive leronlimab in advance of their pending surgery and then start an ICI after surgery. This study is predicated on the prior observation of CNS penetration of leronlimab in macaques, as well as the potentially peripheral site of activity of ICI on T Cells in patients who had their protected tumor microenvironment disrupted while receiving leronlimab prior to surgery.

Other Pre-Clinical and Clinical Projects

We are pleased to share that the Alzheimer’s study at Cornell University Medical Center in New York has received both FDA and IRB approval, a “kickoff meeting” was just conducted, and enrollment will begin in the coming weeks. As previously noted, this study has been funded by an outside foundation to whom we are very grateful, but that wishes to remain anonymous at this time.

Additionally, the LATCH study with Dr. Jonah Sacha and his team at Oregon Health & Science University has been updated and is now ready for IRB and FDA submission. The study will further explore the role of leronlimab in the potential cure of HIV+ patients who receive a stem cell transplant from CCR5+ donors. We were also able to work with Dr. Sacha to arrange for commitments from outside foundation(s) to fund the costs of this study.

Pending Publications

Our top publication priority remains a comprehensive TNBC manuscript that includes the clinical and PD-L1 data presented at ESMO, as well as recent laboratory data generated by Dr. Richard Pestell that appears to reinforce our belief in leronlimab as a paradigm shift in solid tumor oncology. The initial draft of the manuscript will be ready for internal review in the coming weeks.

The Company has also prepared a case report of a patient with mTNBC whose cancer had

spread to both brain and lungs, but who is alive today without evidence of disease, almost 5 years after receiving fourth-line treatment with leronlimab plus atezolizumab. That manuscript will be submitted for peer review shortly.

The company is also preparing a safety manuscript summarizing the safety data in almost 1,600 patients who have now been treated with leronlimab in CytoDyn-sponsored studies.

The company's manuscript describing the results of CytoDyn's prior study in patients with Metabolic Dysfunction-Associated Steatohepatitis was recently accepted for publication.

Finally, we have recently submitted two additional manuscripts for peer-review, including:

- A manuscript of a preclinical study of CRC performed at the Cleveland Clinic, which demonstrated a significant reduction in lung metastasis in mice treated with leronlimab.
- A manuscript summarizing results from SMC Laboratories detailing the effects of leronlimab on liver fibrosis, inflammation, and fat.

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