December 16, 2025

December 2025 Letter to Shareholders

VANCOUVER, Washington, Dec. 16, 2025 (GLOBE NEWSWIRE) --

Dear Shareholders,

As we close out the year and step with confidence and purpose into 2026, I want to extend my sincere appreciation for your support, patience, and continued belief in CytoDyn's (the "Company") mission. I will remember 2025 as the year in which we first presented our astonishing survival observations and compelling data on the emerging role of leronlimab in solid tumor oncology. This past year has been one of disciplined execution, operational rebuilding, and meaningful scientific progress. Today, we are a far stronger, more focused, and more capable company than we were twelve months ago.

In February, we announced increased survival rates in patients with metastatic Triple-Negative Breast Cancer ("mTNBC") who were treated with leronlimab in prior studies. In May, after further evaluation of the underlying data and treatment profiles on the group of long-term survivors, we shared our exciting new proposed mechanism of action ("MOA") for leronlimab. Among the long-term survivors with sustained remission, we observed three common factors: (i) treatment with leronlimab, (ii) subsequent expression of PD-L1 levels on circulating tumor cells above a common threshold, and (iii) treatment with an immune checkpoint inhibitor ("ICI"). All five patients who were treated in this manner are alive today, five years later, and three of these individuals currently show no evidence of disease. The patient profiles and underlying data, albeit retrospective, suggest that leronlimab can convert "cold" (PD-L1–negative) tumors into "hot" (PD-L1–positive) tumors by blocking CCR5, thereby enabling a potential "prime and pair" regimen in which leronlimab primes the tumor microenvironment which then allows ICIs to unleash an immune response.

Once prospectively confirmed, leronlimab's ability to induce a "hot" tumor microenvironment should be a game changer in solid tumor oncology. This is our top clinical priority, and data supporting this concept are being collected in our active Phase 2 colorectal cancer ("CRC") trial and will be collected in our Phase 2 mTNBC trial set to commence in 2026.

Calendar 2025 in Review

Throughout 2025, our team delivered on several critical priorities designed to restore momentum and position CytoDyn for long-term success:

> **Operational Strengthening.** We advanced essential regulatory preparations, refined our clinical strategy, and improved internal processes. This included strengthening data integrity standards, enhancing trial oversight, and engaging more consistently and constructively with regulators and investigators.
>
> **Clinical Program Advancement.** Our scientific team made significant progress across our therapeutic focus areas. While early-stage milestones rarely generate headlines, this foundational work ultimately determines a biotech company's trajectory.

By improving study design, aligning with clinical experts, and prioritizing areas of unmet need, we have created a roadmap that is realistic, executable, and value-creating. A detailed Clinical Update supplement is attached at the end of this letter.

Financial Discipline. 2025 was marked by prudent financial stewardship. We remained focused on extending our runway, improving our cost structure, and ensuring that resources are directed toward programs with the highest probability of success and the greatest potential benefit for patients.

The progress we made this year is tangible. As we continue towards prospectively confirming our MOA theories, the progress above is not theoretical and our team has positioned the company to move confidently into its next phase. We have tightened operations, clarified our approach, strategically resolved legal issues, and established the infrastructure needed to deliver meaningful results. Our optimism for 2026 is grounded firmly in the work completed in 2025.

Looking Ahead to Calendar 2026

As we enter 2026, CytoDyn stands on the cusp of several important clinical and regulatory inflection points. I am optimistic about the near-term milestones ahead, including:

- Advancements in our ongoing clinical studies
- Near-term data readouts towards prospectively confirming our MOA theories
- Continued progress in regulatory interactions that may unlock new clinical pathways
- Strengthening relationships with key clinicians, investigators, and potential partners

With the fundamentals in place and our programs advancing, 2026 is poised to be the year CytoDyn re-enters the industry conversation with force and credibility. We believe the coming year will showcase:

- Strong clinical execution
- Clear scientific validation
- Data-driven milestones
- Pathways that may enable new opportunities with clinicians, researchers, and industry partners

Biotech requires rigor, patience, and adherence to the regulatory process, but we have every reason to believe that the groundwork laid in 2025 will begin to show tangible results in 2026.

Closing Thoughts

Thank you for standing with us. Thank you for believing in our mission to develop therapies with the potential to improve lives. And thank you for your continued commitment to CytoDyn as we enter what I believe will be the most important and transformative year in our company's history. We are ready. We are focused. And in 2026, we intend to make waves.

Wishing everyone a safe and joyful holiday season,
Jacob Lalezari, MD

CEO

Note Regarding Forward-Looking Statements
This news release contains forward-looking statements relating to, among other things, the mechanism of action of leronlimab, 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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Clinical Update
– December 2025 –

Our Phase II study of patients with mCRC was launched in July 2025, to evaluate the safety and efficacy of leronlimab (350 mg versus 700 mg) added to a backbone of Bevacizumab and Tipiracil. As of this writing, the study has enrolled 16 patients with another 23 patients in screening. Based upon current projections, we anticipate 20 patients to be enrolled by the end of the year, and to have the trial fully enrolled in or around May 2026.

Early results from the mCRC trial have been very encouraging, and we have already submitted abstracts for at least two presentations on the CRC study in 2026– one presentation on biomarker results, and a second focused on clinical outcomes. In addition, the study design is being amended so that patients who have a clinical progression will have the option of adding an ICI to their treatment regimen. As a result, the final CRC study design will allow us to evaluate leronlimab both as a "stand-alone" agent on its own (added to the background regimen) and as a "prime and pair" agent used in conjunction with ICIs.

We recently received feedback from FDA on two proposed protocols for patients with mTNBC, including a Phase II study combining leronlimab with ICIs as well as an Expanded Access Program (EAP). We are incorporating FDA's helpful comments and will be submitting revised protocols for both initiatives in the near future.

The Phase 2 trial in patients with mTNBC will enroll individuals onto a dosing regimen of weekly leronlimab along with chemotherapy for several cycles after which time they will be randomized to immediate versus deferred treatment with an ICI. The primary endpoint of the

study will be clinical evaluation of Overall Response Rate (ORR) with secondary endpoints including both Progression-Free Survival (PFS) and Overall Survival (OS). Two exploratory endpoints will include evaluation of changes in PD-L1 on circulating tumor cells as well as changes in circulating tumor DNA (ctDNA). This study is intentional and dynamic, meant to provide prospective confirmation of the “prime and pair” paradigm that we believe will be of particular interest to potential industry partners, as well as evaluate leronlimab’s potential for monotherapy benefit.

With Every Patient (WEP Clinical) has been engaged to serve as our clinical research organization (CRO) for the EAP, and we expect to open the program for patient referral in or around February 2026, assuming FDA’s allowance of our revised protocol submission. In addition to providing compassionate access to patients who have exhausted other treatment options and are otherwise unable to participate in our upcoming Phase 2 trial, the EAP program will serve as another potential avenue to observe PD-L1 induction following treatment with leronlimab, and thereby – in theory – opening a treatment pathway towards sustained remission when combined with an ICI. As previously shared, we are grateful to a high-net worth individual who has agreed to cover the cost of the first 20 patients enrolled in this two-year program.

In 2025 there was a marked increase in incoming requests for CytoDyn to collaborate with investigators from a variety of academic centers. I am pleased to announce that we are proceeding with four such initiatives, and that all four are being funded in part or entirely by outside third parties. First, an investigator at City of Hope has received institutional approval for a study of subcutaneous leronlimab given in combination with a regimen of chemotherapy administered through the hepatic artery in treatment-naïve patients with mCRC who have metastatic disease confined to the liver. This study seeks to leverage CytoDyn’s previously announced data demonstrating leronlimab’s ability to mitigate liver toxicity in prior preclinical studies, as well as certain preliminary results from the phase II CRC study. This study is intended to provide CytoDyn with important tumor tissue from patients treated with leronlimab. This tissue will enable us to correlate tumor levels of PD-L1 with levels concurrently measured in blood on circulating tumor cells. This tissue will also provide CytoDyn the opportunity to further clarify and understand the leronlimab-induced changes in the tumor microenvironment (TME) that lie at the heart of the “Prime and Pair” paradigm.

Second, in keeping with our focus on solid tumor oncology, CytoDyn is collaborating with several academic centers on a pilot study of patients with recurrent Glioblastoma. This study proposes to treat patients with leronlimab in advance of their scheduled surgery for recurrent disease. After surgery, patients will begin treatment with an ICI in the hope that a leronlimab-disrupted TME can then be treated with an ICI and provide clinical benefit to patients.

In addition to the above, CytoDyn has been working with several investigators on two exciting projects outside oncology. Our collaborator at Cornell has finalized a 12-week pilot study of leronlimab in patients with mild to moderate Alzheimer’s Disease. All the necessary approvals have been received, and the study is scheduled to begin screening after requisite equipment is installed at Cornell in April 2026.

Lastly, we continue work with Dr. Jonah Sacha, and others at Oregon Health Sciences University and the University of Washington, on an HIV cure project involving stem cell transplantation. The final protocol is now complete and submission to both institutional IRBs

and FDA will commence shortly.



Source: CytoDyn Inc.