Celyad Oncology

Letter to Shareholders

2022

Dear Shareholder,

Over 2021, the hard work and dedication of the entire Celyad Oncology team has helped us to continue to make steady progress advancing our mission to develop next-generation allogeneic CAR T candidates that offer new therapeutic options to cancer patients with poor prognosis. Our development pipeline has continued to transition to an allogeneic strategy centered around i) our single-step engineering, All-in-One vector approach and ii) our proprietary non-gene edited technologies including short hairpin RNA (shRNA) and T cell receptor Inhibitory Molecule (TIM). Throughout the past twelve months, we've announced encouraging clinical data from our programs at major scientific conferences and further built our position as a leader in the field of allogeneic CAR T cell therapies.

Reflecting and Driving the “CAR” Forward

At Celyad Oncology (the “Company”), we have made it a priority to leverage our expertise, experience and technology to establish the Company as a leader in the investigational allogeneic CAR T therapy space. Although the patient-derived autologous approach has been successful in some malignancies, there remains a great need for therapies in other kinds of tumors that could benefit from the “off-the-shelf” allogeneic approach.

Right now, we are particularly excited about our shRNA technology platform. This differentiated technology allows us to modulate gene expression without the need for gene-editing or the use of multiple vectors. Importantly, with shRNA technology, we can adjust expression of key genes to create investigational allogeneic cell therapies. With shRNA, we seek to interfere with the expression of the CD3ζ component of the T cell receptor complex, while improving the overall profile of these cutting-edge candidates with less complexity of multi-vector approaches. We truly believe there’s tremendous potential for implementing shRNA technology in the development of next-generation allogeneic CAR T cell therapies and we’re only beginning to scratch the surface.

Focused on Execution

In 2021, we reported several important clinical milestones as we continued to deliver on our goal of advancing our pipeline of investigational allogeneic CAR T therapies.

At the 63rd American Society of Hematology (ASH) Annual Meeting and Exposition we presented the latest clinical data from the dose-escalation segment of the IMMUNICY-1 Phase 1 trial evaluating CYAD-211, a shRNA-based anti-BCMA allogeneic CAR T candidate. These data showed evidence of initial clinical activity for CYAD-211 in patients with relapsed or refractory multiple myeloma (r/r MM) with a good tolerability profile, including no evidence of Graft-versus-Host Disease, or GvHD, and preliminary cell engraftment. The next segment of the IMMUNICY-1 study will evaluate CYAD-211 following enhanced lymphodepleting regimens with the aim to improve cell persistence and potentially maximize the clinical benefit of anti-BCMA cell therapy. In addition, the IMMUNICY-1 protocol allows for redosing of CYAD-211 in certain patients. Enrollment in the IMMUNICY-1 trial is ongoing with additional data expected in the second half of 2022.

In December 2021, we announced dosing the first patient in the KEYNOTE-B79 Phase 1b trial evaluating our TIM-based NKG2D receptor allogeneic candidate, CYAD-101, with MSD’s anti-PD-1 therapy, KEYTRUDA® (pembrolizumab), in patients with refractory metastatic colorectal cancer (mCRC) with microsatellite stable (MSS)/mismatch-repair proficient disease. Unfortunately, February 2022 brought an unexpected challenge, and we voluntarily paused this trial and subsequently announced an FDA hold. Patient safety is our number one priority, and we are currently working to investigate these events. We plan to have an update for stakeholders in the future.

In July 2021, we introduced our armored CAR T franchise centered on the proinflammatory cytokine

interleukin-18, or IL-18. IL-18's dual mechanism of action directly potentiates the anti-cancer activity of CAR T cells while also altering the balance of pro- and anti-inflammatory cells within the tumor microenvironment. Currently, we are conducting Investigational New Drug (IND)-enabling studies for CYAD-203, our first shRNA-based allogeneic armored CAR T candidate engineered to co-express IL-18 with the NKG2D CAR receptor. We anticipate the submission of an IND application for CYAD-203.

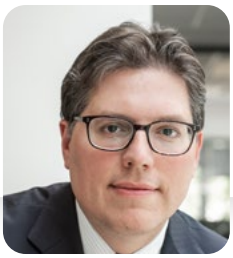
Lastly, regarding our next-generation autologous NKG2D CAR T candidate CYAD-02, we announced the latest data from the program at ASH in December 2021. Results from the CYCLE-1 trial evaluating CYAD-02 for the treatment of relapsed or refractory (r/r) acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) indicated that a single shRNA can target two independent genes to optimize CAR T cell phenotype. We believe clinical data from CYCLE-1 support the potential and versatility of the shRNA platform while further validating its uniqueness among currently available gene-expression control technologies for the development of next-generation CAR T therapies.

Focused on the Future

As we evaluate our progress, it is important to remember that the true potential for our company and its technologies reaches far beyond the current development pipeline. I'm deeply grateful to all of our team members who tirelessly deliver each and every day with dedication in pursuit of our mission to develop innovative cell therapies against cancer.

The value and opportunity provided by our team, development pipeline and underlying platform technologies are key points of focus for our investors. We remain steadfast in the goal of furthering our pipeline of investigational allogeneic CAR T therapies this new year. We appreciate the ongoing support of our investors as we execute on our growth strategy.

On behalf of the entire Celyad Oncology team and board members, I wish you and your loved ones a happy, healthy and fulfilling 2022!



Regards,
Filippo Petti,
CEO Celyad Oncology

Check out our Financial Calendar here:
celyad.com/investors/

Celyad Oncology

MORE INFORMATION ON:
www.celyad.com

FOR SHAREHOLDERS:
www.celyad.com/investors

CONTACT:
investors@celyad.com