



Celyad
Oncology

2023

Letter to Shareholders

Dear Shareholder,

2022 has been a crossroad year for Celyad Oncology ("the Company"), with important changes and turning points.

Whilst our clinical programs had clear potential, as we pursued clinical development over the years, we systematically discovered more effective ways of furthering our goal to impact cancer with CAR T-cell therapy. Also, Celyad transitioned from autologous to allogeneic approaches, which changed our company dynamic. We faced challenges stemming from insufficient clinical efficacy as well: our allogeneic program, CYAD-211, as evaluated in the IMMUNICY-1 trial, did not demonstrate sufficient clinical efficacy to be pursued into Phase II studies without changing the treatment scheme or eligibility criteria. In addition, serious adverse events were reported in the KEYNOTE-B79 trial of our lead allogeneic program, CYAD-101, which resulted in a temporary suspension of the trial. Here, as with CYAD-211, we could only pursue the program with a change of the eligibility criteria, which would have resulted in additional delays and costs.

This stream of events in the first months of 2022 led to the decision by the board of directors to reshape the strategy of the Company, to focus on its core assets, its world class research unit and intellectual property. A re-organization plan was put in place in June, under the leadership of Michel Lussier, who stepped down as chairman of the board and assumed the position of CEO ad interim, succeeding our then CEO and CFO, Filippo Petti. Hilde Windels, a member of our board since 2017, stepped in as Chair.



Michel Lussier
Co-Founder, Interim
CEO



Hilde Windels

Chair of the Board

“ We believe that Celyad is well prepared and has the relevant unique assets and know how to create significant shareholder value in the next few years “

The Company executed an in-depth organizational transformation in the second half of the year:

- Significant cost cutting and cost saving initiatives have been implemented in order to strictly allocate the resources of the Company to the activities and programs that could potentially bring maximum value to shareholders. To that end, Celyad Oncology discontinued non-strategic R&D programs and opted not to begin any new clinical trial development;
- A hiring freeze was implemented as of March 2022;
- 26 employees and four contractors were transferred in October to Cellistic™ (a division of Ncardia) following the acquisition of Celyad's Cell Therapy Manufacturing Unit (CTMU) by Ncardia Belgium SA;
- Effective 9 January 2023, the clinical team (eight employees) joined the organization of ProPharma Group Holdings LLC, a global reputed CRO with whom Celyad has simultaneously entered into a service agreement for support relating to the closing of its clinical trials. The clinical trials remain under the Company's responsibility as sponsor while the clinical workforce has been transferred to said partner to secure a seamless closing of the clinical studies, preserving the best interests of the patients and investigational sites; and
- The Company also sold several assets (e.g. equipment & refurbishment for 1,3Mi€ in order to relocate to a nearby facility, better suited to the Company's future needs).

All initiatives undertaken by the Company since spring 2022 have created a projected cash burn reduction that would allow a forecasted cash runway extension by approximately 12 months, up to the fourth quarter of 2023, without any external financing.

Starting in 2023, Celyad Oncology will now entirely focus on its new business strategy moving forward with an adapted organization and, we believe, the right headcount to successfully deliver on it.

On the financing side, in the thir quarter of 2022, the Company engaged Van Lanschot Kempen N.V. to evaluate several financing options.

In summary, while our clinical results have not lived up to expectations, we are hopeful for the many patients who have been successfully treated in these programs and the solid foundation it has created to move these therapies further. We believe that our clinical accomplishments, strengthened with the current and future research efforts, can lead to commercially successful products.

Having dealt with the 2022 challenges, Celyad has now successfully reinvented itself as a leaner, more agile organization with three clear objectives:

- 1) Strengthen its research focus centered around NKG2D, B7-H6 and shRNA platforms;
- 2) Maximize its valuable IP estate and
- 3) Drive innovation through strategic collaborations.

We believe that Celyad is well prepared and has the relevant unique assets and know how to create significant shareholder value in the next few years.

Michel Lussier
Co-Founder, Interim CEO

Hilde Windels
Chair

Corporate strategy

- The Company has implemented a strategic shift from an organization focused on clinical development to one prioritizing R&D discovery and leveraging its Intellectual Property (IP) estate through partnerships, collaborations and license agreements.
- The Company has compiled a foundational and broad IP estate that controls key aspects of developing therapies in the allogeneic cell therapy space.
- The patents around allogeneic chimeric antigen receptor (CAR) T-cell therapies and NKG2D-based therapies provide an avenue to develop intellectual property programs and to partner with outside parties around the licensing of these patents.

Pursuing a Differentiated Strategy for CAR Ts



- All-in-one vector approach
- Validated proprietary allogeneic technologies
 - shRNA – short hairpin RNA
 - TIM – TCR Inhibitory Molecule
- Differentiated targets & multi-targeting

Non-gene Edited shRNA-Powered & TIM Technologies



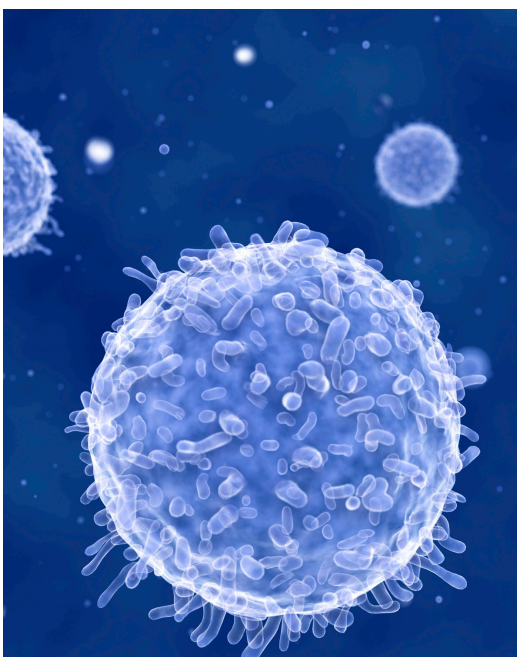
- Offers dynamic platform for the development of allogeneic or autologous CAR T-cells
- shRNA technology allows to multiplex by knocking down multiple gene targets of interest simultaneously
- shRNA and TIM proof-of-concept completed in humans

Robust Intellectual Property Estate



- Multiple foundational U.S. patents
 - NKG2D receptor-based cell therapies
 - TCR-deficient T-cell compositions
 - IP estate broadly covering allogeneic therapies
- Promising avenue to partner with outside parties around licensing

Current challenges



Over the past decades, CAR T-cell therapy has emerged as a realistic treatment paradigm for patients with advanced cancer disease.

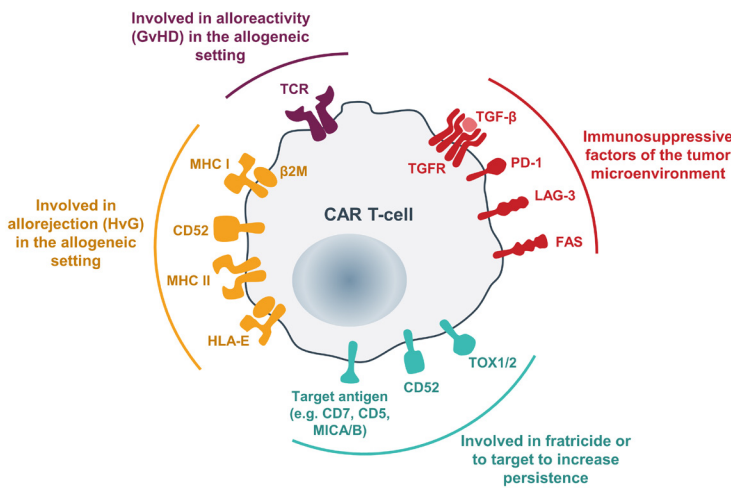
However, despite this success, several challenges remain:

- All CAR T-cell products with demonstrated clinical benefit are indicated for a very limited number of B-cell malignancies. There is an urgent need for targets specific to tumor cells from other indications.
- An inherent downside of CAR T-cells targeting a single antigen is that cells not expressing the antigen will not be targeted, which may lead to resistance or relapse after a first response of short duration.
- Solid cancers, and some hematological indications, sculpt a tumor microenvironment (TME) that not only restricts lymphocyte trafficking, but also downregulates their activity, expansion and persistence at the tumor site.
- Autologous CAR T-cells also come with a lag time between collection of the patient's T-cells and infusion of the CAR T-cell product, but also product quality variations, and logistical challenges.

Our R&D goals

The Company is implementing a differentiated and innovative strategy, tackling the major current limitations of CAR T-cell therapies. This strategy includes:

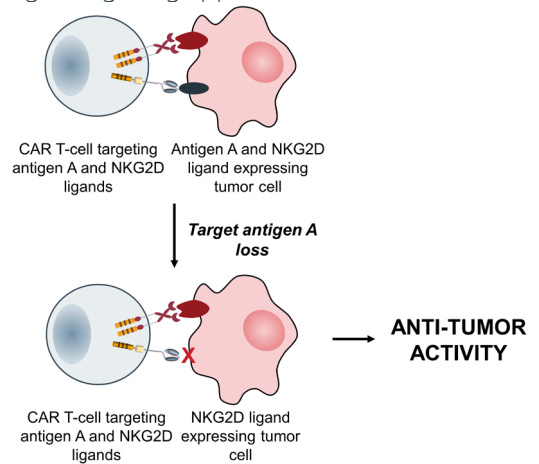
- **A multiplexing approach of short hairpin RNAs (shRNA)**, allowing multiple genes, including essential and functional genes, to be modulated simultaneously.



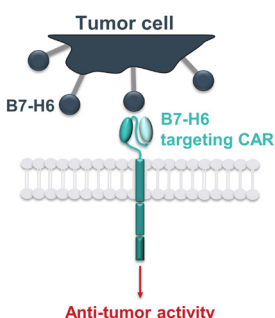
- ✓ shRNA is a small piece of RNA that can decrease gene expression, effectively turning genes off
- ✓ Modulation with shRNA allows targeting of essential functional genes and genes whose partial expression is required
- ✓ Ability to optimize CAR T-cell features, persistence, efficacy or ability to evade complex or immunosuppressive tumor microenvironments, for both allogeneic or autologous products
- ✓ Complementary to our “all-in-one vector approach” to express multiple shRNAs in a single construct within a single transduction step
- ✓ Proof-of-concept of the shRNA technology in humans to prevent alloreactivity of allogeneic CAR T-cells

- **The dual CAR development of a next-generation NKG2D-based CAR**, which may help to overcome resistance and immune escape often observed with traditional single targeting approaches.

- ✓ With a dual CAR, several antigens can be targeted together by the same CAR product so that if there is a loss of one antigen, there are still others that can work to kill the cancer cells
- ✓ A dual CAR with NKG2D capabilities and targeting another undisclosed antigen could be used to decrease risk of relapse or resistance often observed with traditional single-targeting CAR T approaches
- ✓ May move the CAR T-cell landscape beyond B-cell malignancies



- **The development of B7-H6-targeting immunotherapies**, as the Company believes that B7-H6 is an underappreciated target that could change the paradigm of cell therapy due to its broad expression in a large variety of cancers.



- ✓ Attractive approach to target a broad range of cancers including lymphoma, ovarian, gastric or breast cancers
- ✓ In cancers, B7-H6 expression is associated with tumor progression, poor prognosis and lymph node metastasis
- ✓ Targeting B7-H6 has the advantage to promote only activating functions; hence, it may be used to recognize and kill tumor cells
- ✓ May move the CAR T-cell landscape beyond B-cell malignancies

2023 Outlook

Over the years, Celyad Oncology has appreciated the long-lasting support of our shareholders. We now find ourselves at a pivotal time in the Company's history with a new vision and strategy for 2023 and beyond.

The Company will continue to leverage the dynamic potential of the shRNA platform, and to explore options to tackle the major current limitations of CAR T-cell therapies through 2023.

Celyad Oncology is of the opinion that it will potentially create more shareholder value by licensing its patent estate and further strengthening its research efforts to improve the differentiated nature of its platforms.

The entire Celyad Oncology team and Board members wish you and your loved ones a happy, healthy and fulfilling 2023!

Financial calendar 2023

March 23rd – Full Year 2022 Financial Results

May 5th – First Quarter 2023 Business Update

May 5th – Annual Shareholders Meeting

August 3rd – First Half 2023 Interim Financial Results

November 9th – Third Quarter 2023 Business Update

CONTACT:

investors@celyad.com

 [@CELYADSA](https://twitter.com/CELYADSA)

 [@CELYAD](https://www.linkedin.com/company/celyad)

MORE INFORMATION ON:

www.celyad.com

MORE INFORMATION FOR SHAREHOLDERS ON:

www.celyad.com/investors



Celyad
Oncology