Celyad Provides Update on Allogeneic CAR-T Franchise including CYAD-101 and shRNA Platform at the 2020 ASCO Virtual Scientific Program

- First-in-class TIM-based non-gene edited allogeneic CAR-T candidate, CYAD-101, shows encouraging clinical activity with no evidence of graft-versus-host disease in relapsed/refractory metastatic colorectal cancer patients
- Two patients achieved a confirmed partial response and nine patients achieved stable disease, leading to a disease control rate of 73%
- Overall safety and clinical activity data are HLA-independent indicating that CYAD-101 cells can be used in a broad patient population regardless of the HLA haplotype
- Expansion cohort of the alloSHRINK trial evaluating CYAD-101 following FOLFIRI preconditioning chemotherapy is expected to begin in the fourth quarter 2020
- shRNA platform for next-generation allogeneic CAR-T candidates provides proof-of-principle to simultaneously knockdown up to four genes in a single construct
- Management to hold a conference call on Monday, June 1st, at 2 p.m. CEST/ 8 a.m. EDT

Mont-Saint-Guibert, Belgium - Celyad (Euronext Brussels and Paris, and Nasdaq: CYAD), a clinical-stage biopharmaceutical company focused on the development of CAR-T cell therapies, today announced updates from the company’s allogeneic programs, including additional data from the Phase 1 alloSHRINK trial evaluating the T cell receptor (TCR) inhibitory molecule (TIM)-based, non-gene edited allogeneic CAR-T candidate, CYAD-101, for the treatment of metastatic colorectal cancer (mCRC), and the company’s short hairpin RNA (shRNA) platform underpinning the next-generation, non-gene edited CYAD-200 series of CAR-T candidates. These data were presented at the 2020 American Society of Clinical Oncology (ASCO) Virtual Scientific Program from May 29-31, 2020.

Dr. Frédéric Lehmann, VP of Clinical Development at Celyad, commented, “The latest safety and clinical activity data from the alloSHRINK trial in metastatic colorectal cancer patients further demonstrate CYAD-101’s differentiated profile as an allogeneic CAR-T candidate. The absence of clinical evidence of graft-versus-host-disease (GvHD) for CYAD-101, which co-expresses the NKG2D receptor with our novel, TIM technology used to knockdown signalling of the TCR complex, confirms the potential of non-gene edited approaches for the development of allogeneic CAR-T candidates. Taking these positive clinical data into account, we have decided to broaden the program to include evaluating CYAD-101 following FOLFIRI chemotherapy in refractory patients as an expansion cohort of the alloSHRINK trial. Overall, treatment of advanced metastatic colorectal cancer patients beyond second line regimens remains a high unmet medical need, and we believe CYAD-101 could offer a unique immunotherapeutic approach to treat this incurable disease.”

Dr. David Gilham, CSO of Celyad, stated, “CYAD-101 has pioneered the potential for non-gene edited approaches for the development of allogeneic CAR-T candidates, and we are excited to build upon this strong
position with our shRNA technology platform. Preclinical data reported during ASCO over the past few days confirm the ability of a single shRNA hairpin to provide prolonged TCR knockdown, which our first shRNA-based allogeneic candidate, CYAD-211. In addition, the data demonstrated the breadth and depth of the shRNA platform, including the concurrent knockdown of up to four genes. We believe combining the knockdown potential of the platform with additional construct enhancements provides tremendous therapeutic optionality to our non-gene edited CYAD-200 series of CAR-T candidates.”

**alloSHRINK Phase 1 Trial Update**

**Background**
- To date, a total of 15 patients with relapsed/refractory mCRC who progressed after previous treatment with oxaliplatin-based or irinotecan-based chemotherapies have been enrolled in the dose-escalation, alloSHRINK Phase 1 trial evaluating three consecutive dose levels of CYAD-101 administered concurrently with FOLFOX chemotherapy. The number of prior therapies received by patients enrolled in the trial ranged from one to six with a mean of three.
- All 15 patients were dosed from a single cell bank of CYAD-101 that was generated in advance from two manufacturing runs each using a fraction of an apheresis from a single healthy donor.

**Safety and Tolerability**
- No clinical evidence of GvHD has been observed following 44 injections of CYAD-101. We believe these data continue to support the ability of the company’s novel inhibitory peptide TIM to reduce signaling of the TCR complex through a non-gene edited approach.
- Treatment with CYAD-101 following FOLFOX preconditioning chemotherapy was observed to be well-tolerated. Seven of the 15 patients enrolled in the trial reported at least one treatment-related adverse event (AE), however, all AEs reported were grade 1 or 2, including one patient who experienced cytokine-release syndrome (grade 1). No patient discontinued treatment due to AEs.

**Clinical Activity**
- Encouraging anti-tumor activity was observed in the trial with two patients who achieved a confirmed partial response (PR) according to RECIST 1.1 criteria, including one patient with a KRAS-mutation, the most common oncogenic alteration found in all human cancers. In addition, nine patients achieved stable disease (SD), with seven patients demonstrating disease stabilization lasting more than or equal to three months of duration.
- No correlation was observed between clinical responses and the degree of human leukocyte antigen (HLA) matching between patients and CYAD-101 donor cells, indicating that CYAD-101 can be used in a broad patient population regardless of the HLA haplotype.

**Next Steps**
- An expansion cohort of alloSHRINK trial will evaluate CYAD-101 following FOLFIRI (combination of 5-fluorouracil, leucovorin and irinotecan) preconditioning chemotherapy in refractory mCRC patients, at the recommended dose of one billion cells per infusion. Enrollment in the expansion cohort of the trial is expected to begin during the fourth quarter of 2020.
shRNA Platform and CYAD-200 Series

Background

- In October 2018, the company announced an exclusive agreement with Horizon Discovery Group for the use of its shRNA technology to generate a novel, next-generation, non-gene-edited allogeneic platform for CAR-T therapies. Horizon Discovery’s SMARTvector technology to express shRNA was optimized by Celyad to knockdown the TCR complex in allogeneic CAR-T therapies as well as to target a broad range of proteins.

shRNA Platform

- shRNA platform coupled with company’s all-in-one vector approach is designed to provide flexibility, versatility and efficiency in designing novel, allogeneic CAR-T candidates through single step engineering process.
- Lead shRNA-based allogeneic candidate CYAD-211, targeting B-cell maturation antigen (BCMA) for the treatment of relapsed/refractory multiple myeloma, which uses a single hairpin to knockdown the CD3ζ component of the TCR complex, is expected to enter clinical trials by year-end 2020.
- Next-generation candidates exploring two shRNA knockdowns are currently under development.
- Continued preclinical evaluation of the shRNA platform demonstrates proof-of-principle that the concurrent knockdown of four genes using an optimized framework is feasible.
- Combining shRNA knockdown with additional functional components should offer therapeutic optionality to non-gene edited allogeneic CYAD-200 series of product candidates.

Conference Call and Webcast Details

Celyad will host a conference call to discuss the update from ASCO on Monday, June 1, 2020 at 2 p.m. CEST / 8 a.m. EDT. The conference call can be accessed through the following numbers:

- United States: +1 877 407 9208
- International: +1 201 493 6784
- Conference ID: 13703684

The conference call will be webcast live and can be accessed here. The event will also be archived and available on the “Events & Webcasts” section of the company’s website. Please visit the website several minutes prior to the start of the broadcast to ensure adequate time for registration to the webcast.

About CYAD-101 and alloSHRINK Trial

CYAD-101 is an investigational, non-gene edited, allogeneic (healthy donor derived) CAR-T candidate engineered to co-express a chimeric antigen receptor based on NKG2D, a receptor expressed on natural killer (NK) cells that binds to eight stress-induced ligands and the novel inhibitory peptide TIM (TCR Inhibitory Molecule). The expression of TIM reduces signalling of the TCR complex, which is responsible for graft-versus-host disease.

alloSHRINK is an open-label, dose-escalation Phase 1 trial assessing the safety and clinical activity of three consecutive administrations of CYAD-101 every two weeks administered concurrently with FOLFOX (combination of 5-fluorouracil, leucovorin and oxaliplatin) chemotherapy in patients with refractory mCRC. In the expansion cohort of the trial, CYAD-101 will be administered concurrently with FOLFIRI.
About shRNA Platform and CYAD-200 Series

The company is focused on the development of its proprietary non-gene edited allogeneic short hairpin RNA (shRNA) SMARTvector technology platform through the CYAD-200 series of candidates. The company is currently evaluating several shRNA-based allogeneic CAR-T candidates, including CYAD-211, an allogeneic CAR-T candidate targeting B-cell maturation antigen for the treatment of relapsed/refractory multiple myeloma.

About Colorectal Cancer

Colorectal cancer is the third most common type of cancer among both men and women worldwide and is the fourth most common in terms of mortality. In 2018, approximately 1.8 million people were diagnosed with colorectal cancer, with about 140,000 and 500,000 diagnoses in the United States and Europe, respectively. According to data from ASCO, approximately 40% of patients are diagnosed with early-stage, localized-stage disease. The five-year survival rate of localized disease is approximately 90%. In patients where the cancer has spread to distant parts of the body, as in metastatic colorectal cancer, the five-year survival rate drops to approximately 15%.

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About Celyad

Celyad is a clinical-stage biopharmaceutical company focused on the development of specialized CAR-T cell-based product candidates and utilizes its expertise in cell engineering to target cancer. Celyad’s CAR-T cell platform has the potential to treat a broad range of solid and hematologic tumors. The company’s lead clinical candidate, CYAD-01, an autologous NKG2D-based CAR-T therapy, is currently being evaluated in several Phase 1 clinical trials to assess safety and clinical activity for the treatment of hematological malignancies, such as acute myeloid leukemia, and solid cancers, such as metastatic colorectal cancer. Celyad is also developing CYAD-101, an investigational, non-gene edited, allogeneic (donor derived) NKG2D-based CAR-T candidate, which is currently being evaluated in a Phase 1 trial for the treatment of patients with metastatic colorectal cancer. Celyad was founded in 2007 and is based in Mont-Saint-Guibert, Belgium, and New York, NY. Celyad’s ordinary shares are listed on the Euronext Brussels and Euronext Paris exchanges, and its American Depositary Shares are listed on the Nasdaq Global Market, all under the ticker symbol CYAD. Celyad has received funding from the Walloon Region (Belgium) to support the advancement of its CAR-T cell therapy programs.

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Forward-looking statements

This release may contain forward-looking statements, including statements regarding: the safety and clinical activity of CYAD-01, CYAD-02, CYAD-100 Series and CYAD-200 Series; statements regarding the ongoing and planned clinical development of CYAD-01, CYAD-02, CYAD-100 Series and CYAD-200 Series, including the timing of trials, enrolment, data readouts and presentations; the clinical and commercial potential of CYAD-01, CYAD-02, CYAD-100 Series and CYAD-200 Series; the success of the OptimAb manufacturing system; the ongoing and planned clinical and
commercial potential and development of Celyad’s shRNA technology; Celyad’s financial condition, results of operation and business outlook. Forward-looking statements may involve known and unknown risks, uncertainties and other factors which might cause actual results, financial condition and liquidity, performance or achievements of Celyad, or industry results, to differ materially from those expressed or implied by such forward-looking statements. In particular it should be noted that the data summarized above are preliminary in nature. There is limited data concerning safety and clinical activity following treatment with the CYAD-01, CYAD-02, CYAD-100 Series and CYAD-200 Series product candidates. These results may not be repeated or observed in ongoing or future studies involving the CYAD-01, CYAD-02, CYAD-100 Series and CYAD-200 Series drug product candidates. These forward-looking statements are further qualified by important factors and risks, which could cause actual results to differ materially from those in the forward-looking statements, including statements about: the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs; our ability to advance drug product candidates into, and successfully complete, clinical trials; our ability to successfully manufacture drug product for our clinical trials, including with our OptimAb manufacturing process and with respect to manufacturing drug product with the desired number of T cells under our clinical trial protocols; our reliance on the success of our drug product candidates, including our dependence on the regulatory approval of CYAD-01, CYAD-02, CYAD-100 Series and CYAD-200 Series in the United States and Europe and subsequent commercial success of CYAD-01, CYAD-02, CYAD-100 Series and CYAD-200 Series, both of which may never occur; the timing or likelihood of regulatory filings and approvals; our ability to develop sales and marketing capabilities; the commercialization of our drug product candidates, if approved; the pricing and reimbursement of our drug product candidates, if approved; the implementation of our business model, strategic plans for our business, drug product candidates and technology; the scope of protection we are able to establish and maintain for intellectual property rights covering our drug product candidates and technology; our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights and proprietary technology of third parties; cost associated with enforcing or defending intellectual property infringement, misappropriation or violation; product liability; and other claims; regulatory development in the United States, the European Union, and other jurisdictions; estimates of our expenses, future revenues, capital requirements and our needs for additional financing; the potential benefits of strategic collaboration agreements and our ability to maintain and enter into strategic arrangements; our ability to maintain and establish collaborations or obtain additional grant funding; the rate and degree of market acceptance of our drug product candidates, if approved; our financial performance; developments relating to our competitors and our industry, including competing product candidates and statements regarding future revenue, hiring plans, expenses, capital expenditures, capital requirements and share performance and the impact of the novel coronavirus, COVID-19, including potential effects on our business, clinical trials, supply chain and manufacturing capabilities. A further list and description of these risks, uncertainties and other risks can be found in Celyad’s U.S. Securities and Exchange Commission (SEC) filings and reports, including in its Annual Report on Form 20-F filed with the SEC on March 25, 2020 and subsequent filings and reports by Celyad. Given these uncertainties, the reader is advised not to place any undue reliance on such forward-looking statements. These forward-looking statements speak only as of the date of publication of this document and Celyad’s actual results may differ materially from those expressed or implied by these forward-looking statements. Celyad expressly disclaims any obligation to update any such forward-looking statements in this document to reflect any change in its expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based, unless required by law or regulation.