Press Release
10 December 2019
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Celyad Presents Update on r/r AML and MDS Program at 61st ASH Annual Meeting

- *Future development of relapsed/refractory (r/r) acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) program to be underpinned by proprietary OptimAb manufacturing process*
- *Enrollment of DEPLETHINK trial evaluating CYAD-01 following preconditioning chemotherapy continues, while THINK trial progresses to expansion segment with plans to evaluate monotherapy CYAD-01 produced with OptimAb manufacturing process*
- *CYCLE-1 trial evaluating next-generation, NKG2D-based CAR-T therapy CYAD-02 following preconditioning chemotherapy on track to begin enrollment in early 2020*
- *Preliminary results from the r/r AML and MDS program using the OptimAb manufacturing process are expected by the end of first half 2020*

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 to the company's autologous NKG2D-based CAR-T development program for the treatment of relapsed/refractory (r/r) acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) at the American Society of Hematology (ASH) 61st Annual Meeting, which is being held from December 7-10, 2019 in Orlando, Florida.

Filippo Petti, CEO of Celyad, commented, *"Over the past few months we have worked diligently to transition our proprietary OptimAb manufacturing process to become the cornerstone of our autologous CAR-T program for the treatment of relapsed/refractory acute myeloid leukemia and myelodysplastic syndromes. We are encouraged by the body of data generated to date by our lead autologous candidate CYAD-01 for the treatment of AML and MDS, especially given its tolerability profile and anti-leukemic activity."*

"We are excited to further evaluate our NKG2D-based CAR-T approach using our OptimAb manufacturing process, which generates a higher frequency of less differentiated CAR-T cells that exhibit enhanced anti-tumor activity in preclinical studies. Overall, we believe the process gives us the best opportunity for success across both autologous product candidates, CYAD-01 and CYAD-02. Along with our ongoing DEPLETHINK trial, the key next steps for our broad r/r AML and MDS program include the expansion of the THINK trial and initiation of the CYCLE-1 trial as we look to establish NKG2D as an important target for the treatment of difficult-to-treat malignancies", continued Mr. Petti.

CYAD-01 THINK Phase 1 Trial

- Sixteen patients have been enrolled to date in the trial evaluating CYAD-01 administered as a multiple injection with a biweekly schedule and an additional nine patients have been enrolled in the dose dense (weekly) schedule in the dose escalation segment of the trial

- CYAD-01 without preconditioning chemotherapy was generally reported to be well-tolerated, with 11 out of 25 patients experiencing grade 3/4 treatment-related adverse events (AEs). Cytokine release syndrome (CRS) occurred in 13 patients, with four grade 3 and two grade 4 events, which showed rapid resolution following the appropriate treatment, including tocilizumab. Two dose-limiting toxicities were reported at dose level 3 (3 billion cells per infusion), including one CRS grade 4 (biweekly) and one CRS grade 3 (dose dense schedule). No treatment-related neurotoxicity AEs were reported
- Overall, eight patients out of 15 evaluable patients treated with CYAD-01 produced with the prior manufacturing process demonstrated anti-leukemic activity. Five out of the eight patients exhibited an objective response. In addition, one patient is exhibiting disease stabilization of over three months
- Patients treated within the CYAD-01 dose-dense (weekly) schedule cohorts of the trial did not demonstrate an improvement in clinical outcome as compared to patients treated with the biweekly dosing schedule. However, patients enrolled in the dose-dense schedule cohorts appeared to have greater bone marrow blasts infiltration and to be more pancytopenic at baseline compared to patients enrolled in the biweekly dose escalation segment of the trial
- Most of the anti-leukemic activity observed in the trial, except for the two patients who bridged to an allogeneic human stem cell transplant, experienced a short durability of response
- To date, anti-leukemic activity appears predominantly observed in patients initially diagnosed with non-adverse (ELN 2017, AML) or non-very high (IPSS-R, MDS) risk stratification categories. Additional patients are needed in the trial to better assess the observation
- Company plans to progress to the expansion segment of the THINK trial to further evaluate CYAD-01 produced with the OptimAb manufacturing process. Enrollment in the expansion segment of the trial is expected to begin in first quarter 2020 with preliminary data anticipated by the end of first half 2020

<u>CYAD-01 DEPLETHINK Phase 1 Trial</u>

- Nine patients have been enrolled in the trial evaluating CYAD-01 produced with the prior mAb manufacturing process following preconditioning chemotherapy cyclophosphamide and fludarabine, or CyFlu, at the first two dose levels of the dose escalation segment of the trial
- CYAD-01 produced with the mAb manufacturing process was generally reported to be well-tolerated following preconditioning chemotherapy. At the first CYAD-01 infusion of the consolidation cycle (3 billion cells per infusion), one patient experienced both grade 4 cytokine release syndrome (CRS) and grade 3 CAR-T cell-related encephalopathy and another patient experienced grade 3 CRS. Both patients recovered following the appropriate treatment, including tocilizumab
- Preconditioning chemotherapy led to improved, dose-dependent engraftment of CYAD-01 cells as compared to cells infused with no preconditioning
- To date, no objective response has been observed at the first two dose levels of the trial in patients treated with CYAD-01 produced with the mAb manufacturing process
- In September 2019, the company announced the successful administration of CYAD-01 produced with the OptimAb manufacturing process to a patient enrolled in cohort 3 (300 million cells per infusion) of the trial

- Enrollment in the trial is ongoing with plans to dose escalate up to one billion cells per infusion in cohort 4. Preliminary data evaluating CYAD-01 produced with the OptimAb manufacturing process from cohorts 3 and 4 are expected by the end of first half 2020

CYAD-02 CYCLE-1 Phase 1 Trial

- In November 2019, the company initiated the dose-escalation Phase 1 CYCLE-1 trial (NCT04167696), which will evaluate the safety and clinical activity of the next-generation, autologous NKG2D-based CAR-T candidate CYAD-02, produced with the OptimAb manufacturing process following preconditioning chemotherapy CyFlu in patients with r/r AML and MDS
- CYAD-02 incorporates shRNA SMARTvector technology licensed from Horizon Discovery to target the NKG2D ligands MICA and MICB. shRNA-mediated knockdown of MICA and MICB expression on NKG2D CAR-T cells has been shown to enhance *in vitro* expansion of the CAR-T cells and enhanced engraftment and persistence in preclinical models as compared to CYAD-01 produced with the mAb process
- Enrollment in the CYCLE-1 trial is expected to begin in early 2020 with preliminary data anticipated during second half 2020

About THINK Phase 1 Trial

The THINK trial (NCT03018405) is an open-label, dose-escalation Phase 1 trial assessing the safety and clinical activity of multiple CYAD-01 administrations without prior preconditioning. The dose escalation segment of the trial evaluated three dose levels (300 million, 1 billion and 3 billion cells per infusion) of one cycle of three CYAD-01 administrations with two-week intervals. In 2018, the THINK trial was amended to add two cohorts to assess a more frequent dosing schedule of CYAD-01 for the treatment of r/r AML. The cohorts will evaluate six injections of CYAD-01 without preconditioning over two months of administration. The first cycle includes three infusions of CYAD-01 separated by one-week intervals. The second cycle includes three infusions of CYAD-01 separated by two-week intervals. Patients will either receive 1 billion cells per infusion (Cohort 10) or 3 billion cells per infusion (Cohort 11). The primary endpoint of the trial is safety and secondary endpoints include clinical activity and pharmacokinetics.

About DEPLETHINK Phase 1 Trial

In October 2018, Celyad initiated the DEPLETHINK Phase 1 trial (NCT03466320). The open-label, dose-escalation trial is designed to evaluate a single infusion of CYAD-01 following treatment with the standard preconditioning regimen of cyclophosphamide (300 mg/m²) and fludarabine (30 mg/m²), or CyFlu. The trial includes two different intervals between lymphodepletion and administration of CYAD-01. In addition, the trial is evaluating three dose levels of CYAD-01 including 100 million, 300 million and 1 billion cells per infusion, respectively. The primary endpoint of the trial is safety and secondary endpoints include clinical activity and pharmacokinetics.

About OptimAb Manufacturing Process

Celyad's proprietary OptimAb manufacturing process utilizes a shortened cell culture and incorporates a selective PI3K inhibitor. This results in a product that is enriched for T cells with a memory-like phenotype. Preclinical data demonstrate that NKG2D-based CAR-T cell therapies produced using the OptimAb manufacturing process drive improved anti-tumor activity in an aggressive AML model compared to alternative manufacturing process.

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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 therapy, 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 Depository 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 and CYAD-02; statements regarding the ongoing and planned clinical development of CYAD-01 and CYAD-02, including the timing of trials, enrollment, data readouts and presentations; the clinical and commercial potential of CYAD-01 and CYAD-02; and the OptimAb manufacturing process. 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-101 and CYAD-02 drug product candidates. Prior clinical and preclinical results may not be repeated or observed in ongoing or future clinical studies involving the CYAD-01 and CYAD-02 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-101 and CYAD-02 in the United States and Europe and subsequent commercial success of CYAD-01, CYAD-101 and CYAD-02, 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 therapies and statements regarding future revenue, hiring plans, expenses, capital expenditures, capital requirements and share performance. 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 April 5, 2019 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.