

## Celyad Provides Clinical Update and Strategic Outlook for 2018

*15 Patients treated in THINK Trial as of December 31, 2017,  
promising signs of clinical activity observed*

*Additional clinical trials planned in patients with  
acute myeloid leukemia (AML) and colorectal cancer (CRC)*

*Improved manufacturing process now in the clinic*

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**Mont-Saint-Guibert, Belgium** - Celyad (Euronext Brussels and Paris, and NASDAQ: CYAD), a clinical-stage biopharmaceutical company today provided an update on its ongoing Phase 1 clinical trial, called THINK (THerapeutic Immunotherapy with NKG2D), to assess the safety and clinical activity of its lead drug product candidate, CYAD-01, in seven refractory cancers, including both solid and hematologic cancers. As of December 31, 2017, Celyad had treated 15 patients with CYAD-01 in the THINK trial. In six of the 10 patients treated at the per-protocol intended dose, Celyad observed signs of clinical activity ranging from Stable Disease (SD) to Complete Response (CR). In all cases, CYAD-01 was administered as a monotherapy without chemotherapy preconditioning. Based on the promising interim results of the THINK trial, the company plans to further evaluate CYAD-01 in a series of additional Phase 1 clinical trials in patients with acute myeloid leukemia (AML) and colorectal cancer (CRC).

Celyad also announced that drug product manufactured using an improved manufacturing process designed to significantly increase the yield of T cells in the drug product that is produced, is now in the clinic. The first patient in the THINK trial to be administered drug product manufactured using the new manufacturing process was treated in late January 2018.

**Christian Homsy, CEO of Celyad commented:** *"We are very pleased with our progress in the clinic during 2017, especially the observations of Stable Disease and Complete Response achieved at the lower doses and without chemotherapy preconditioning. Encouraged by these results, we are rapidly developing a robust clinical development plan for this product candidate in both AML and CRC. We are likewise excited to see drug product produced using our improved manufacturing process in the clinic. We anticipate that this process will enable us to significantly increase the yield of T cell expansion in the drug product we produce, while at the same time reducing process complexity and cost. We look forward to advancing our clinical development efforts in 2018, as we seek to leverage our expertise in cell therapy technology for the benefit of critically ill patients in need."*

The company also reported that, based on preliminary unaudited information and management estimates, at December 31, 2017, it had cash and cash equivalents and short term investments of approximately €34 million and is reconfirming guidance of a cash run rate into the first half of 2019.

### **THINK Trial Update (all data is as of December 31, 2017)**

As of December 31, 2017, Celyad had treated 15 patients with CYAD-01 drug product in the THINK trial. Patients have been treated at the first and/or second dose level in both the solid and hematological tumor cohort of the dose escalation part of the trial. The company is currently enrolling patients for the third dose level phase in the solid tumor cohort and completing the second dose level phase in the hematological arm.

As of December 31, 2017, Celyad had not observed the same Grade 4 or above adverse event in two or more patients and no patient experienced a Grade 5 adverse event. No patient experienced an adjudicated Grade 4 or higher CRS adverse event or neurotoxic adverse event.

Of the 15 patients treated as of December 31, 2017, 10 were dosed at the per-protocol intended dose and five were treated at a dose lower than the per-protocol intended dose using drug product manufactured using a prior manufacturing method. In six of the 10 patients treated at the per-protocol intended dose Celyad observed signs of clinical activity ranging from Stable Disease (SD) to Complete Response (CR). Signs of clinical activity were observed in patients with AML, CRC and ovarian cancer. No signs of clinical activity were observed in patients treated with a dose lower than the per-protocol intended dose.

In all three AML patients treated at the per-protocol intended dose Celyad observed signs of clinical activity. A fourth AML patient was treated at a dose lower than the per-protocol intended dose and did not show signs of clinical activity. In two of four CRC patients treated at the per-protocol intended dose, Celyad observed signs of clinical activity. These two patients showed SD at the three-month follow-up date, both receiving the first dose level. A fifth CRC patient was treated at a dose lower than the per-protocol intended dose and did not show signs of clinical activity.

### **Manufacturing Update**

Until recently, CYAD-01 drug product was manufactured using a process which did not consistently produce the required number of T cells in the drug product for the higher doses, resulting in some cases in an inability to manufacture drug product consistent with the protocol for the THINK trial. All 15 patients treated in the THINK trial as of December 31, 2017 were treated with drug product manufactured using this process. Of these 15 patients, 10 were dosed at the per-protocol intended dose and five were treated at a dose lower than the per-protocol intended dose due to an inability to obtain sufficient cell numbers in the drug product using this manufacturing method.

In response to these manufacturing challenges, Celyad modified the manufacturing process to include a monoclonal antibody (mAb) that inhibits NKG2D expression on the T cell surface during production. This method has the potential to yield significantly higher cell numbers. The THINK protocol has been amended for this new approach, and in the first three patient lot produced since this process was implemented, a very high cell yield was obtained.

The first patient in the THINK trial to be administered drug product manufactured using the mAb process was treated in late January 2018. The data from this patient is still emerging, but based on a preliminary review, the patient experienced an adverse event consistent with those observed in patients treated with drug product manufactured using the prior method, specifically hypoxia, which may or may not be adjudicated to be the result of CRS. Given that the drug product was administered in late January, it is too early to assess signs of clinical activity in this patient.

### **C-Cure**

Until mid-2016, Celyad was focused on the development of a cardiovascular drug product candidate called C-Cure, an autologous cell therapy for the treatment of patients with ischemic heart failure. This program was funded in part through various research programs from the Walloon Region of Belgium. In June 2016, Celyad reported topline results from a Phase 3 clinical trial for this drug product candidate. Following the announcement of these results, the company explored strategic options to further develop and commercialize C-Cure, while the company focused on its CAR-T oncology drug product candidates. In December 2017, Celyad notified the Walloon Region of its decision not to exploit the results of this program in exchange for a cancellation of the loans of the Region to the Company.

Version française disponible sur le site de Celyad [www.celyad.com](http://www.celyad.com)

Nederlandstalige versie beschikbaar op de website van Celyad [www.celyad.com](http://www.celyad.com)

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### **About Celyad**

Celyad is a clinical-stage biopharmaceutical company focused on the development of specialized CAR-T cell based therapies. Celyad utilizes its expertise in cell engineering to target cancer. Celyad's Natural Killer Receptor based T-Cell (NKR-T) platform has the potential to treat a broad range of solid and hematologic tumors. Its lead oncology candidate, CYAD-01 (CAR-T NKG2D), has been evaluated in a single dose escalation Phase 1 clinical trial to assess the safety and clinical activity of multiple administrations of autologous CYAD-01 cells in seven refractory cancers including five solid tumors (colorectal, ovarian, bladder, triple-negative breast and pancreatic cancers) and two hematological tumors (acute myeloid leukemia and multiple myeloma). Celyad was founded in 2007 and is based in Mont-Saint-Guibert, Belgium, and Boston, Massachusetts. 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.



Press Release  
1 February 2018  
09:15 am CEST

**About the THINK Trial**

In December 2016, Celyad initiated the THINK (THERapeutic Immunotherapy with NKr-2) trial, a multinational (E.U./U.S.), open-label Phase 1 clinical trial to assess the safety and clinical activity of multiple administrations of CYAD-01 in seven metastatic tumor types, including five solid tumors (colorectal, ovarian, bladder, triple-negative breast and pancreatic cancers) and two hematological tumors (AML and MM) in patients who did not respond to or relapsed after first and second line therapies. CYAD-01 is administered as a monotherapy in patients without chemotherapy preconditioning.

The trial contains two consecutive segments: a dose escalation segment with two arms (one in solid tumor types and one in hematological tumor types) at three dose levels adjusted to body weight (up to 3x10<sup>8</sup>, 1x10<sup>9</sup> and 3x10<sup>9</sup> CAR-T NKr-2 cells) and an expansion phase that includes seven tumor types (five solid tumors and two hematological tumors). At each dose, the patients are intended to receive three successive administrations of the specified dose, two weeks apart. The dose escalation part of the study is expected to enroll up to 36 patients while the extension phase is planned to enroll up to 86 patients. The primary endpoint of the dose escalation segment is a safety endpoint—the occurrence of dose limiting toxicities in patients during the treatment until 14 days after the last treatment. The primary endpoint in the expansion segment is objective response rate.

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*This press release contains inside information within the meaning of Regulation (EU) No 596/2014 of the European Parliament and of the Council of 16 April 2014 on market abuse (market abuse regulation).*

**Forward-looking statements**

This release may contain forward-looking statements, including statements regarding the safety and efficacy of CYAD-01 and the new mAb manufacturing method used to manufacture this drug product candidate; statements concerning the ongoing and planned clinical development of CYAD-01; and statements concerning our estimated balance of cash and cash equivalents at December 31, 2017 and cash run rate guidance. 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 interim data summarized above are current as of December 31, 2017 and are preliminary in nature. The THINK trial is not complete. There is limited data concerning safety and clinical activity following treatment with the CYAD-01 drug product candidate. These results may not be repeated or observed in ongoing or future studies involving the CYAD-01 drug product candidate. 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 new mAb 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 in the United States and Europe and subsequent commercial success of CYAD-01, 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 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 4, 2017 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.