Press Release
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# Celyad initiates second dose escalation in THINK trial in first US patient

- Initiation of the THINK trial in the US at Roswell Park Cancer Institute
- Dosing of the first patient of the second dose ($1x10^9$) in solid tumor arm
- Favorable safety profile reported on all patients treated with CAR-T NKR-2

**Mont-Saint-Guibert, Belgium** - Celyad (Euronext Brussels and Paris, and NASDAQ:CYAD), a leader in the discovery and development of engineered cell therapies, today announced the dosing of the first patient of the second dose in the solid tumor arm of its THINK trial (**TH**erapeutic **I**mmunotherapy with **NK**R-2). This first ovarian cancer patient has been dosed at Roswell Park Cancer Institute (Buffalo, New York).

At the first solid tumor dose-level, one pancreatic and two colorectal cancer patients were successfully dosed. None of these patients experienced dose limiting adverse events.

THINK is a multinational open-label Phase I study to assess the safety and clinical activity of multiple administrations of autologous NKR-2 T-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). These cancer indications were selected based on strong preclinical evidence and NKG2D ligand expression.

The THINK trial is being conducted in the US and in Europe. It contains a dose escalation and an extension stage. The dose escalation is conducted in parallel in the solid and liquid cancer groups, while the extension phase will evaluate in parallel each tumor independently.

The dose escalation design includes three dose levels adjusted to body weight: up to $3x10^8$, $1x10^9$ and $3x10^9$ NKR-2 T-cells. At each dose, the patients receive three successive administrations, two weeks apart, of NKR-2 T-cells at the specified dose.

“The opening of the first U.S. arm of the THINK study is an exciting milestone, and one we are very proud to contribute to”, **said Kunle Odunsi, MD, PhD, FRCOG, FACOG, Deputy Director of Roswell Park Cancer Institute and the co-Principal Investigator leading Roswell Park’s involvement in the international basket trial**. “NKR-2 represents a unique approach to CAR T-cell therapy, and we hope that our efforts help to establish a new treatment option that will benefit many people with cancer”. Dr. Odunsi is also Chair of Gynecologic Oncology, M. Steven Piver Professor of Gynecologic Oncology and Executive

Director of the Center for Immunotherapy at the Buffalo, N.Y., comprehensive cancer center.

**Dr. Frédéric Lehmann, VP Clinical Development and Medical Affairs at Celyad added:** "Preliminary results from the first dose-level are encouraging, further reinforcing the favorable safety profile of NKR-2. The THINK study is progressing very well and we look forward to the completion of the dose-escalation stage of the trial and the initiation of the expansion segments to confirm the encouraging clinical signal seen in our previous Phase I study. The active participation of a first key cancer institute in U.S. with the NKR-2 manufacturing in Europe demonstrates the ability of Celyad to conduct a global clinical development."

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## About Celyad

Celyad is a clinical-stage biopharmaceutical company focused on the development of specialized cell-based therapies. The Company utilizes its expertise in cell engineering to target severe diseases with significant unmet need, including cancer. Celyad's Natural Killer Receptor based T-Cell (NKR-T) platform has the potential to treat a broad range of solid and liquid tumors. Its lead oncology candidate, NKR-2, has been evaluated in a single dose escalation Phase I clinical trial to assess the safety and feasibility of NKR-2 T-cells in patients suffering from AML or MM. In addition, Celyad has completed a Phase III trial in the EU for its C-Cure® cardiovascular disease candidate in ischemic heart failure. 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 NASDAQ Global Market, all under the ticker symbol CYAD.

For more information about Celyad, please visit: www.celyad.com

## About Celyad's NKR-T Cell Platform

Celyad is developing a unique CAR-T cell using Natural Killer Receptors (NKR) receptors, transduced on T lymphocytes, to target a wide range of solid and hematological tumors. Unlike traditional CAR-T cell therapy, which target only one tumor antigen, Natural Killer (NK) cell receptors enable a single receptor to recognize multiple tumor antigens.

Celyad's lead candidate, NKR-2, is a T-Cell engineered to express the human NK receptor, NKG2D, which is an activating receptor that triggers cell killing through the binding of NKG2D to any of eight naturally occurring ligands that are known to be overexpressed on more than 80% of tumors.

Preclinical results indicate that NKR-2 has multiple mechanisms of actions and goes beyond direct killing by signifying that its encoded T-Cells attack the tumor cells, inhibits the mechanisms that enable tumors to evade the immune system, activates and recruit anti-tumor immune cells and

disrupts the blood supply to the tumor. These mechanisms promote the induction of adaptive immunity, meaning the body develops a long-term cell immune memory against specific tumor antigens of the targeted tumor.

In contrast to traditional CAR-T therapeutic approaches, and based on strong preclinical evidence, Celyad's current NKR-2 program does not employ patient lymphodepleting pre-conditioning, thereby avoiding the toxicities associated with chemotherapy and allowing the immune system to remain intact.

Celyad is developing both autologous and allogeneic NKR-2 administrations. For autologous NKR-2, Celyad collects the patient's own T-Cells and engineers them to express NKG2D in order to target cancer cells effectively. Celyad's allogeneic platform engineers the T-Cells of healthy donors, that also express TCR Inhibitory Molecules (TIMs), to avoid having the engineered donor cells be rejected by the patient's normal tissues (also called Graft vs. Host Disease).

The preclinical research underlying this technology was originally conducted at Dartmouth College by Dr. Charles Sentman and has been published extensively in peer-reviewed publications.

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## Forward looking statements

In addition to historical facts or statements of current condition, this press release contains forward looking statements, including statements about the potential safety and feasibility of CAR-T NKR-2 cell therapy, which reflect our current expectations and projections about future events, and involve certain known and unknown risks, uncertainties and assumptions that could cause actual results or events to differ materially from those expressed or implied by the forward-looking statements. These forward looking statements are further qualified by important factors, which could cause actual results to differ materially from those in the forward-looking statements, including risks associated with conducting clinical trials; the risk that safety, bioactivity, feasibility and/or efficacy demonstrated in earlier clinical or pre-clinical studies may not be replicated in subsequent studies; risk associated with the timely submission and approval of anticipated regulatory filings; the successful initiation and completion of clinical trials, including Phase I clinical trial for CAR-T NKR-2; risks associated with the satisfaction of regulatory and other requirements; risks associated with the actions of regulatory bodies and other governmental authorities; risks associated with obtaining, maintaining and protecting intellectual property, our ability to

enforce our patents against infringers and defend our patent portfolio against challenges from third parties; risks associated with competition from others developing products for similar uses; risks associated with our ability to manage operating expenses; and risks associated with our ability to obtain additional funding to support our business activities and establish and maintain strategic business alliances and business initiatives. A further list and description of these risks, uncertainties and other risks can be found in the Company's Securities and Exchange Commission filings and reports, including in the Company's Annual Report on Form 20-F filed with the SEC on April 8, 2016 and future filings and reports by the Company. 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. The Company 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.