

## Celyad announces the approval to initiate its NKR-2 CAR-T Clinical Trial in Belgium

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**Mont-Saint-Guibert, Belgium** - Celyad (Euronext Brussels and Paris, and NASDAQ: CYAD), a leader in the discovery and development of engineered cell therapies, today announces the approval in Belgium to initiate the THINK clinical trial. THINK is the second clinical trial of its NKR-2 product candidate, a CAR-T cell therapy using NKG2D ligands as a target, to evaluate safety and efficacy in seven cancer indications including both solid and hematological malignancies.

THINK (**T**Herapeutic **I**mmunotherapy with **N**KR-2) is a multinational open-label Phase Ib 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).

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

The dose escalation design will include three dose levels adjusted to body weight: up to  $3 \times 10^8$ ,  $1 \times 10^9$  and  $3 \times 10^9$  NKR-2 T-cells. At each dose, the patients will receive three successive administrations, two weeks apart, of NKR-2 T-cells at the specified dose. The dose escalation part of the study will enroll up to 24 patients while the extension phase would enroll 86 additional patients.

The seven indications evaluated in the THINK trial were selected based on evidence generated in the pre-clinical settings and in the first study recently completed (a Phase I single injection, dose escalation study evaluating NKR-2 T-cells in 12 patients suffering from Acute Myeloid Leukemia (AML) or Multiple Myeloma (MM) at Dana Farber Cancer Institute in Boston, MA, USA).

**Dr. Christian Homsy, CEO of Celyad commented:** *"We are extremely happy to be able to start this next phase of the clinical development program of NKR-2, building on the successful outcome of the single dose, dose escalation trial, to be presented at ASH. We now look forward to treating the first patients in Belgium, and to receiving FDA clearance to initiate the trial at our US-based sites."*

**Dr. Frédéric Lehmann, VP Clinical Development and Medical Affairs at Celyad added:** *"We are excited to initiate this multiple tumor study with key cancer institutions in Belgium. While immunotherapy is rapidly transforming the treatment of patients with cancer, there remains a significant unmet medical need for more effective therapies. It is our hope that Celyad's NKR-2 T-cells have the potential to be truly disruptive in the way we treat cancer and this study is one more step towards that goal."*

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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 Depositary Shares are listed on NASDAQ Global Market, all under the ticker symbol CYAD.

For more information about Celyad, please visit: [www.celyad.com](http://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 NKR-2 T-cell therapy and C-Cure, 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 on-going *ex parte* re-examination of the Company's U.S. patent number 9,181,527, including the risk that the U.S. Patent and Trademark Office may decide to cancel all or a portion of the claims contained therein, 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 III clinical trials for C-Cure® and Phase I clinical trial for 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.

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