Press Release
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Celyad's 2019 R&D Day Highlights shRNA Platform and Pipeline of Next-generation NKG2D-based and Off-the-Shelf Non-gene Edited CAR-T Candidates

- *shRNA platform complements Company's all-in-one-vector approach in the design, discovery and development of next-generation CAR-T candidates*
- *Allogeneic T-cells derived by shRNA targeting show distinctive profile compared to CRISPR-Cas9 gene edited cells in preclinical assays*
- *Plans to initiate several Phase 1 trials to evaluate lead candidates, including next generation, autologous NKG2D-based CYAD-02 and three first-in-class, shRNA-based, non-gene edited allogeneic CAR-T therapies from the CYAD-200 series*

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-based therapies, today presented at R&D Day in New York the continued progress of the its pipeline of proprietary CAR-T therapies for the treatment of hematological malignancies and solid tumors, based on its short hairpin RNA (shRNA) platform.

"We are very pleased with the recent progress of our preclinical CAR-T pipeline," noted Dr. Christian Homsy, CEO of Celyad. *"Together with CYAD-101, our next generation allogenic shRNA platform should allow us to leapfrog the competition in the allogeneic CAR-T landscape. In addition, CYAD-02 has shown encouraging preclinical data of increased CAR-T cell expansion, persistence and anti-tumor efficacy. We continue to tap into our deep expertise and knowledge in cell therapy manufacturing and our all-in-one vector approach provides tremendous flexibility, versatility and efficiency in the design of novel, CAR-T therapies."*

Corporate Updates

- Lead asset CYAD-01 continues to advance in clinical trials for the treatment of patients with relapsed/refractory (r/r) acute myeloid leukemia (AML). The Company reported that additional dosing and schedule optimization are under evaluation in the THINK Phase 1 trial. In addition, the Company reported that interim data from the DEPLETHINK Phase 1 trial evaluating CYAD-01 following preconditioning chemotherapy shows the CAR-T cell therapy is well-tolerated at the initial dose levels following preconditioning chemotherapy. Future clinical updates from the Phase 1 THINK and DEPLETHINK trials are anticipated by mid-2019.
- Company also highlighted its operational excellence for 2018 including a 94% manufacturing success rate and a twofold increase year-over-year in the number of patients treated.

shRNA Platform

- In October 2018, Celyad announced it had entered into 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 optimized by Celyad provides an alternate method to knockout the

TCR complex in allogeneic CAR-T therapies compared to gene editing techniques as well as the specificity to target a broad range of proteins.
- Utilization of the shRNA platform allowed the Company to develop the next generation of autologous, NKG2D-based CAR-T candidate, CYAD-02, and the novel, non-gene edited allogeneic CYAD-200 series of CAR-T candidates.
- In addition, the shRNA platform complements the Company's strong intellectual property of six U.S. patents related to allogeneic T-cell technology and producing TCR deficient cells expressing a CAR construct.

Autologous CAR-T candidate: CYAD-02
- CYAD-02 incorporates shRNA technology to target NKG2D ligands MICA/MICB. In preclinical AML models, CYAD-02 shows an encouraging increase in *in vitro* proliferation and *in vivo* persistence and anti-tumor activity. The Company plans to generate additional preclinical proof-of-concept data for the program throughout 2019 and plans to submit an Investigational New Drug (IND) application for CYAD-02 in first half 2020.

Non-gene edited allogeneic CAR-T candidates: CYAD-200 series
- Celyad utilizes two technologies based on non-gene edited approaches to modulate the T-cell receptor (TCR) complex to generate allogeneic CAR-T therapies. The first approach utilizes our TCR-inhibitor molecule (TIM) and is tailored to our NKG2D-based CAR-T clinical candidate CYAD-101. The second approach leverages shRNA technology exclusively licensed from Horizon Discovery to target the CD3ζ component to knockdown the expression of the TCR/CD3 complex on the surface of the T-cell.
- *In vivo* data demonstrate that shRNA targeting of CD3ζ effectively protects against Graft-versus-Host Disease (GvHD) to a level equivalent to CRISPR-Cas9 based knock-out. Furthermore, results from preclinical tests show significant increase in persistence of allogeneic T cells using shRNA targeting when compared to gene editing technologies, such as CRISPR-Cas9.
- Celyad announced plans to develop three disruptive first-in-class non-gene-edited allogenic CAR-T candidates leveraging the shRNA SMARTvector platform, including:
    - CYAD-211: B-cell maturation antigen (BCMA) targeting CAR-T therapy for the treatment of multiple myeloma, which is expected to enter the clinic by mid-2020.
    - CYAD-221: CD19 targeting CAR-T therapy for the treatment of B-cell malignancies, which is expected to enter the clinic by late 2020.
    - CYAD-231: Dual specific CAR-T targeting NKG2D and an undisclosed membrane protein, which is expected to enter the clinic by early 2021.
- In addition, the company continues to investigate additional undisclosed targets using the shRNA platform to pair with CARs to develop, differentiated next-generation cell therapies for the treatment of both hematological malignancies and solid tumors.

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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 CAR-T cell platform has the potential to treat a broad range of solid and hematologic tumors. Its lead oncology candidate, CYAD-01 (CAR-T NKG2D), is currently being evaluated in a Phase I dose escalation 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). The safety and clinical activity of the CYAD-01 therapy concurrently administered with standard-of-care treatments or preconditioning chemotherapy is also being assessed in a full clinical development program focused on acute myeloid leukemia and 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.

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Forward-looking statements

This release may contain forward-looking statements, including statements regarding the safety and efficacy of CYAD-01 and CYAD-101; the ongoing and planned clinical development of CYAD-01 and CYAD-101, including the timing of trials, enrollment, data readouts and presentations; the clinical and commercial potential of CYAD-01 and CYAD-101 and the adequacy of Celyad's financial resources; Celyad's worldwide development and commercialization rights to CYAD-101; the ongoing and planned clinical and commercial potential and development of its shRNA technology; Celyad's financial condition, results of operation and business outlook; and the effects of Dr. Moore joining Celyad. 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 and CYAD-101 drug product candidates. These results may not be repeated or observed in ongoing or future studies involving the CYAD-01 and CYAD-101 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 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 and CYAD-101 in the United States and Europe and subsequent commercial success of CYAD-01 and CYAD-101, 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 6, 2018 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.