Early signs of clinical activity of NKG2D CAR-T cell (CYAD-01) activity in AML patient
Disclaimer

In addition to historical facts or statements of current condition, this presentation contains forward-looking statements, including statements about the potential safety and feasibility of CYAD-01 cell therapy, including current and planned preclinical and clinical trials for Celyad’s product candidates; the clinical and commercial potential of these product candidates and the adequacy of Celyad’s financial resources; Celyad’s intellectual property portfolio, including plans related thereto; Celyad’s expectations regarding its strategic collaborations and license agreements with third parties, including Novartis, Celdara Medical, and Dartmouth College, and the potential impact of such collaborations on Celyad’s future financial condition; and Celyad’s expected cash burn, which reflect Celyad’s 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 and risks, 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 trials or preclinical studies may not be replicated in subsequent trials or studies; risks associated with the timely submission and approval of anticipated regulatory filings; the successful initiation and completion of clinical trials, including its clinical trials for CYAD-01; 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, Celyad’s ability to enforce its patents against infringers and defend its patent portfolio against challenges from third parties; risks associated with competition from others developing products for similar uses; risks associated with Celyad’s ability to manage operating expenses; and risks associated with Celyad’s ability to obtain additional funding to support its 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 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. 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.
Introduction – Major issues in cancer

- Genetic diversity among patients
- Significant heterogeneity of cancer cells
- Antigens present exclusively in the tumor - neoantigens
- Downregulation of surfaced antigens as an escape mechanism

http://www.nih.gov/about/discovery/chronicdiseases/cancer.htm
NKG2D binds to 8 different known stress ligands expressed in a vast majority of tumors

Expression of at least one of NKG2D ligands:
- Triple negative breast: **88%**
- Colorectals: **88%**
- Ovarian: **68%**
- Bladder: **78%** of the primary tumors and 100% of the metastases
- Pancreatic: **86%**
- NSCLC Lung: **92%** (100% non-squamous NSCLC)


Manuscript in preparation
CYAD-01 activity *in vitro*
CYAD-01 activity *in vivo*

**OVARIAN CANCER**

**LYMPHOMA**

**MULTIPLE MYELOMA**
CYAD-01: Phase I safety trial (CM-CS1)

- **Single administration**, dose-escalation Phase I autologous CAR-T NKG2D study in patients with AML and MM (Dana Farber).

- **Strong safety profile**, including no cell-related neurotoxicity, auto-immunity, or CAR-T related death.

- **Unexpected signs of activity**
  1 AML patient showed stabilization of hematological parameters at 6 months.

Cohort 1: 1x10^6 CYAD-01Cells | 3
Cohort 2: 3x10^6 CYAD-01Cells | 3
Cohort 3: 1x10^7 CYAD-01Cells | 3
Cohort 4: 3x10^7 CYAD-01Cells | 3

Nikiforow S, et al. ASH Session 616 Dec 2016
Murad J. et al. Manuscript submitted
THINK Study (Therapeutic Immunotherapy with NKG2D-based therapy)

- 3 administrations
- Primary Endpoint: Safety & Tolerability
- Secondary Endpoint: Efficacy as Monotherapy (w/o preconditioning)
- Hematological & solid tumors

3 dose levels ($3 \times 10^8$, $1 \times 10^9$ and $3 \times 10^9$)

13 weeks w/o any other non-investigational cancer therapy

- Seven advanced refractory tumor indications
- Global development: EU and USA
First observation of objective clinical response in AML

• 52 y male r/r AML
• FLT3/NPMI mutations
• Received chemotherapy and achieved CR1 but relapsed before allo-HSCT transplantation
CYAD-01 functionality

- **IFN-γ (ng/mL)**
  - No Ab
  - + Ab

- **Cytolytic activity (%)**
  - CYAD-01
  - CYAD-01 + CD314
Relapsed AML patient prior CYAD-01 CAR-T treatment

7% blasts

Ligand expression prior to treatment

Sallman DA, et al, Hematologica, in press
After CYAD-01 treatment: normal cellular phenotype & improved hematopoiesis

- No significant toxicities (grade 3 or above)
- Platelets recover
- Hgb recovery
- BM blasts reduction
- ANC recovery

Sallman DA, et al, Hematologica, in press
SDF-1α levels measured over time

- SDF-1α (CXCL12) is increased in direct relation to CYAD-01 infusions
- SDF-1α is an important agonist of CXCR4

- RANTES (CCL5) is increased in direct relation to CYAD-01 infusions
- RANTES is a T lymphocyte chemotactic factor
- CCR5 expressed on monocytes and T cells

MCP1 (CCL2) levels measured over time

- MCP1 (CCL2) T lymphocyte chemotactic factor
- Increase in direct relation to CYAD-01 infusions

Discussion/Conclusions

- NKG2D CAR T cells (CYAD-01) can target a wide range of solid and liquid cancers *in vitro* and in preclinical models
- An objective response in a patient with r/r AML in the early stages of the THINK trial.
- Serum levels of SDF-1, RANTES and CCL2 modulate in line with dosing of CYAD-01 suggestive of a relationship. The mechanisms relating to these observations remains to be elucidated.
- Additional observations of stable disease in 2 of 4 CRC patients and 1 / 1 ovarian patient
- Encouraging safety and tolerability profile during dose level 1 and 2 of the THINK trial now permitting moving into the final dose level.