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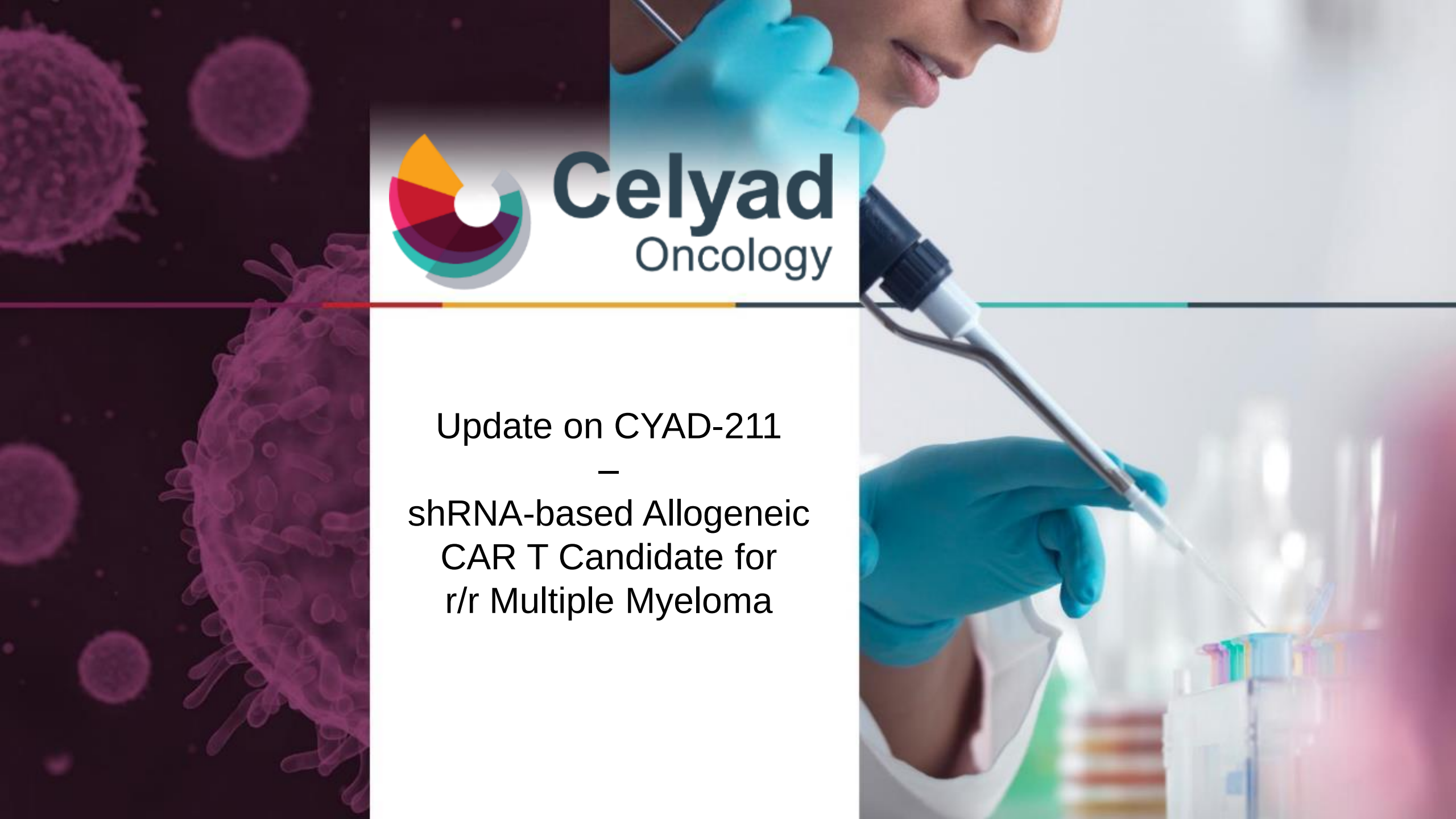
# American Society of Hematology 2020 Virtual Program Update

December 7, 2020

# Forward Looking Statements

This release may contain forward-looking statements, within the meaning of applicable securities laws, including the Private Securities Litigation Reform Act of 1995. Forward-looking statements may include statements regarding: the clinical and preclinical activity of CYAD-02 and CYAD-211. Forward-looking statements may involve known and unknown risks and uncertainties which might cause actual results, financial condition, performance or achievements of Celyad Oncology to differ materially from those expressed or implied by such forward-looking statements. Such risk and uncertainty include the duration and severity of the COVID-19 pandemic and government measures implemented in response thereto. A further list and description of these risks, uncertainties and other risks can be found in Celyad Oncology'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 March 25, 2020 and subsequent filings and reports by Celyad Oncology. These forward-looking statements speak only as of the date of publication of this document and Celyad Oncology's actual results may differ materially from those expressed or implied by these forward-looking statements. Celyad Oncology 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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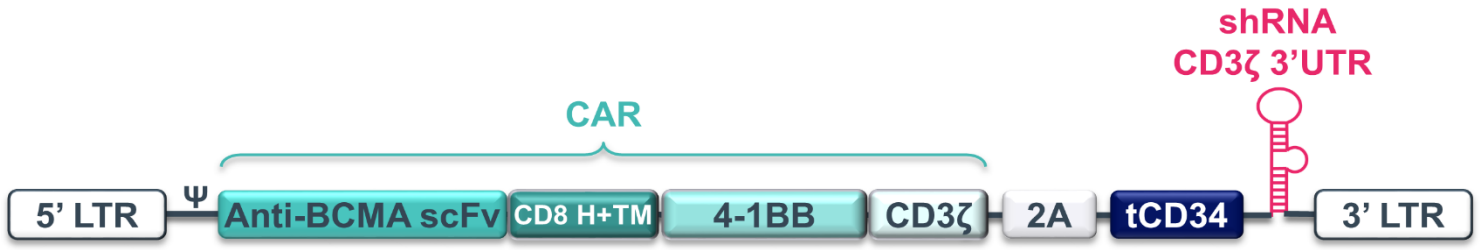
# Update on CYAD-211 – shRNA-based Allogeneic CAR T Candidate for r/r Multiple Myeloma

# CYAD-211 – Anti-BCMA CAR T for Multiple Myeloma

- CYAD-211 is Celyad Oncology's first allogeneic CAR T candidate using shRNA technology utilizing our All-in-One vector approach
- CYAD-211 is an "off-the-shelf" non-gene edited anti-BCMA CAR T candidate which co-expresses:
  - scFv-CD8α-4-1-BB-CD3ζ anti-BCMA CAR
  - Single optimized short hairpin RNA (shRNA) to down-regulate the expression of the T-cell receptor (TCR) CD3ζ subunit, thereby impairing the TCR expression on the surface of the donor T-cells and potential risk of life-threatening graft-versus-host disease (GvHD)
  - Truncated CD34 selection marker

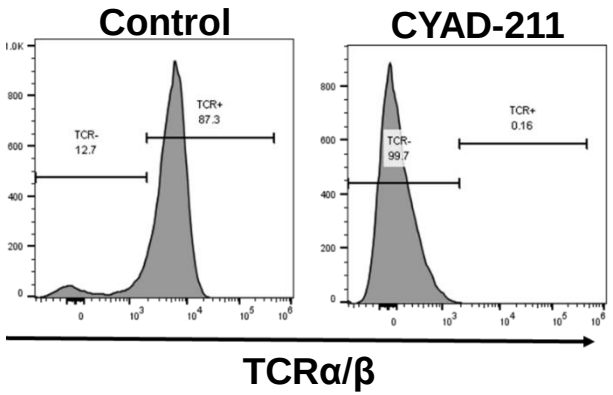



BCMA: B-cell maturation antigen.

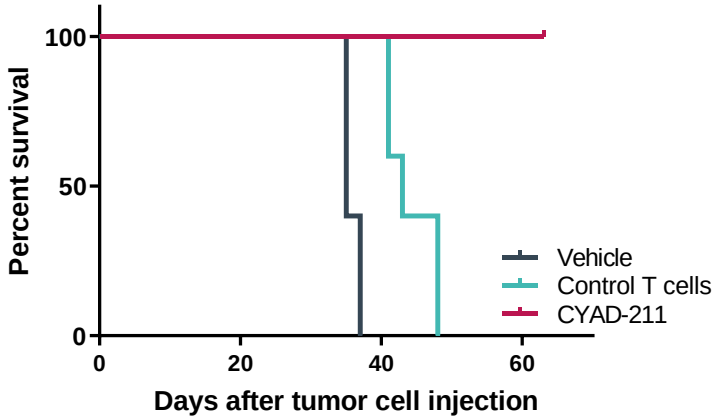
# CYAD-211 – Anti-Tumor Activity With No Evidence of GvHD

- Anti-BCMA CAR T cells with shRNA targeting CD3ζ component exhibit no signs of TCR activation with anti-tumor activity in preclinical models
- No demonstrable evidence of GvHD when CYAD-211 was infused in sub-lethally irradiated NSG mice, the gold standard preclinical model of GvHD, confirming efficient inhibition of alloreactivity

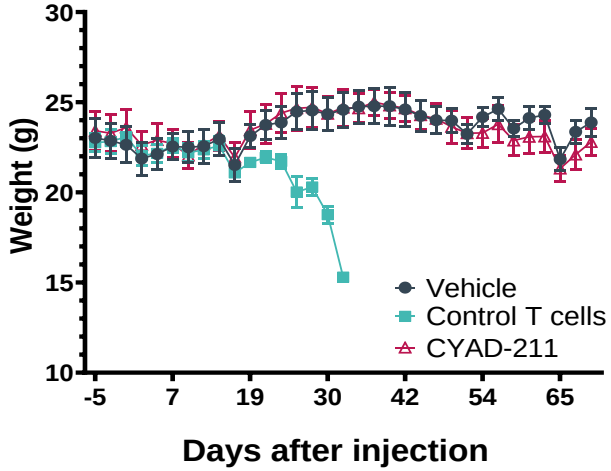
## TCR Knock Down




## Anti-Tumor Activity




## Graft-versus-Host Disease




BCMA: B-cell maturation antigen; GvHD: Graft-versus-Host Disease; shRNA: short hairpin RNA.

# CYAD-211 IMMUNICY-1 – Phase 1 Trial to Determine Recommended Dose

*Open-label, Phase 1 dose-escalation trial in relapsed or refractory multiple myeloma patients*

## Study Design

- Primary objective:
  - Determine the recommended dose of CYAD-211
- Study endpoints:
  - Primary endpoint is the occurrence of dose-limiting toxicities
  - Key secondary endpoints include additional safety parameters, objective responses and duration of responses, and CYAD-211 cell kinetics
- Dose Escalation:
  - $3x10^7$, $1x10^8$ and $3x10^8$ cells per infusion
  - Potential higher dose levels of CYAD-211

## Treatment Schedule


## Key Inclusion Criteria

- Multiple myeloma with relapsed or refractory (r/r) disease to at least two prior treatment regimens
- At least 1 complete cycle of treatment for each prior treatment regimen
- At least 1 response to a prior treatment regimen

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NCT04613557: Safety, Activity and Cell Kinetics of CYAD-211 in Patients With Relapsed or Refractory Multiple Myeloma (IMMUNICY-1).

# CYAD-211 IMMUNICY-1 – Next Steps and Summary

## Next Steps

- First patient from dose level 1 cohort successfully dosed
- Activation of first U.S. clinical sites expected by year-end 2020
- Proof-of-principle (safety and CYAD-211 cell kinetics) data from the initial dose cohorts are expected during first half 2021
- Clinical activity data from the full dose-escalation trial are expected during second half 2021

## Summary

- CYAD-211 is the first non-gene edited allogeneic CAR T cell product candidate based on shRNA technology, incorporating a BCMA-targeting scFv and a shRNA targeting the CD3ζ subunit of TCR complex
- CYAD-211 demonstrated robust anti-tumor activity *in vitro* and *in vivo* concurrent with lack of alloreactivity in preclinical models
- The IMMUNICY-1 clinical study seeks to provide proof of principle that single shRNA-mediated knockdown can generate fully functional allogeneic CAR T cells in humans without GvHD-inducing potential

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BCMA: B-cell maturation antigen; GvHD: Graft-versus-Host Disease; shRNA: short hairpin RNA.

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# Update on CYAD-01 and CYAD-02 – Autologous CAR T Candidates for r/r AML / MDS

# Autologous NKG2D Receptor-Based CAR T Program for r/r AML and MDS

## First-Generation CYAD-01

- Evaluated in both dose-escalation cohorts and dose expansion segment of Phase 1 THINK trial
  - THINK trial assessed the safety and clinical activity of multiple CYAD-01 administrations without prior preconditioning chemotherapy
- Evaluated in dose-escalation Phase 1 DEPLETHINK trial
  - DEPLETHINK trial assessed the safety and clinical activity of CYAD-01 following CyFlu preconditioning

## Next-Generation CYAD-02

- CYAD-02 uses our shRNA technology, a non-gene editing approach, to silence the expression of MICA and MICB with the aim to increase persistence and potency of the NKG2D CAR T cells
  - Improved *in vitro* proliferation, *in vivo* engraftment and anti-tumor activity as compared to CYAD-01 in preclinical models
- Phase 1 CYCLE-1 dose-escalation trial evaluating the safety and clinical activity of CYAD-02 following CyFlu preconditioning

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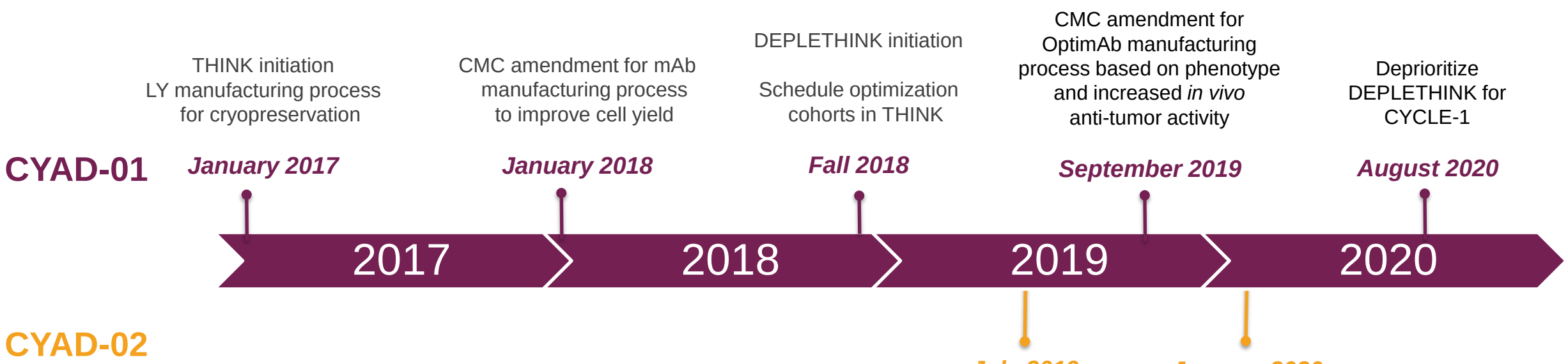
AML: Acute myeloid leukemia; MDS: Myelodysplastic syndrome; r/r: relapse/refractory.
CyFlu: Cyclophosphamide (300 mg/m²) and fludarabine (30 mg/m²)

# Autologous NKG2D Receptor-Based Program Timelines for r/r AML / MDS




- Over the past few years, the company has evaluated several factors in the r/r AML / MDS program:
  - Multiple candidates (first- and next-generation)
  - Multiple dose levels
  - Multiple conditions (monotherapy and preconditioning)
  - Multiple dosing schedules (biweekly and weekly)
  - Multiple manufacturing processes (LY, mAb and OptimAb)

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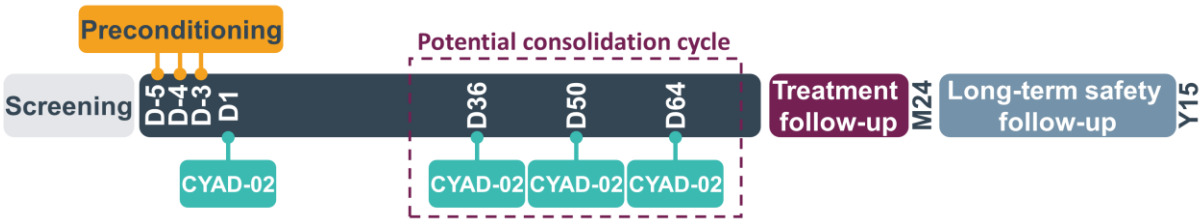
# CYAD-02 CYCLE-1 – Phase 1 Trial to Determine Recommended Dose

*Open-label, Phase 1 dose-escalation trial in relapsed or refractory AML and MDS patients*

## Study Design

- Primary objective:
  - Determine the recommended dose of CYAD-02
- Study endpoints:
  - Primary endpoint is the occurrence of dose-limiting toxicities
  - Key secondary endpoints include additional safety parameters, objective responses and duration of responses, and CYAD-02 cell kinetics
- Dose Escalation:
  - $1x10^8$, $3x10^8$ and $1x10^9$ cells per infusion

## Treatment Schedule




## Patient Population

- AML and MDS with relapsed or refractory (r/r) disease to standard treatment regimens
- Same patient population as THINK and DEPLETHINK Phase I Trials evaluating first-generation CYAD-01

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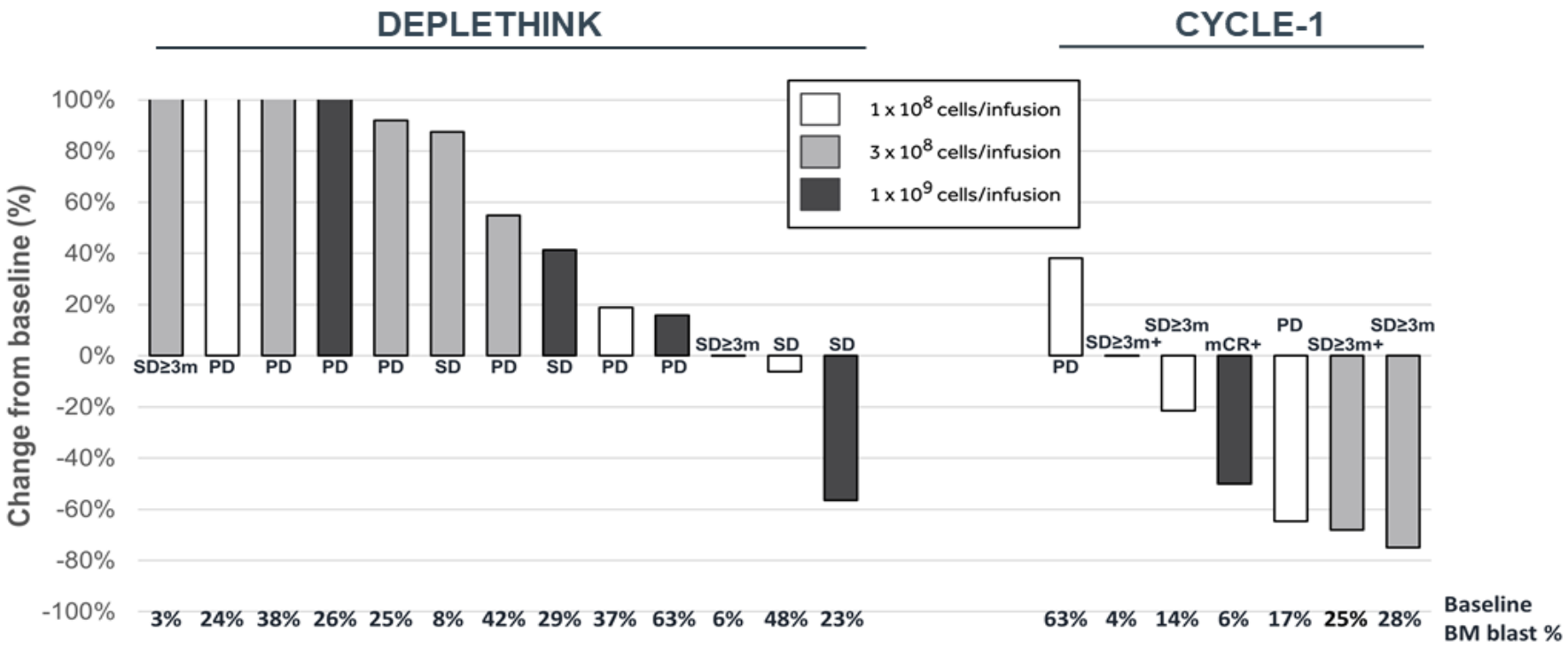
NCT04167696: Study in Relapsed/Refractory Acute Myeloid Leukemia or Myelodysplastic Syndrome Patients to Determine the Recommended Dose of CYAD-02 (CYCLE-1)

# Preliminary Encouraging Clinical Activity from CYCLE-1 Trial

## Impact on Tumor Burden

### CYAD-01

### CYAD-02




+ indicates patient is ongoing.

- Preliminary data to date from CYCLE-1 trial evaluating in r/r AML / MDS patients showed encouraging clinical signals
  - Four out of the seven patients observed to date have at least 50% bone marrow blasts decrease, including a high-risk MDS patient treated at dose level 3 who achieved an objective marrow complete response (mCR)

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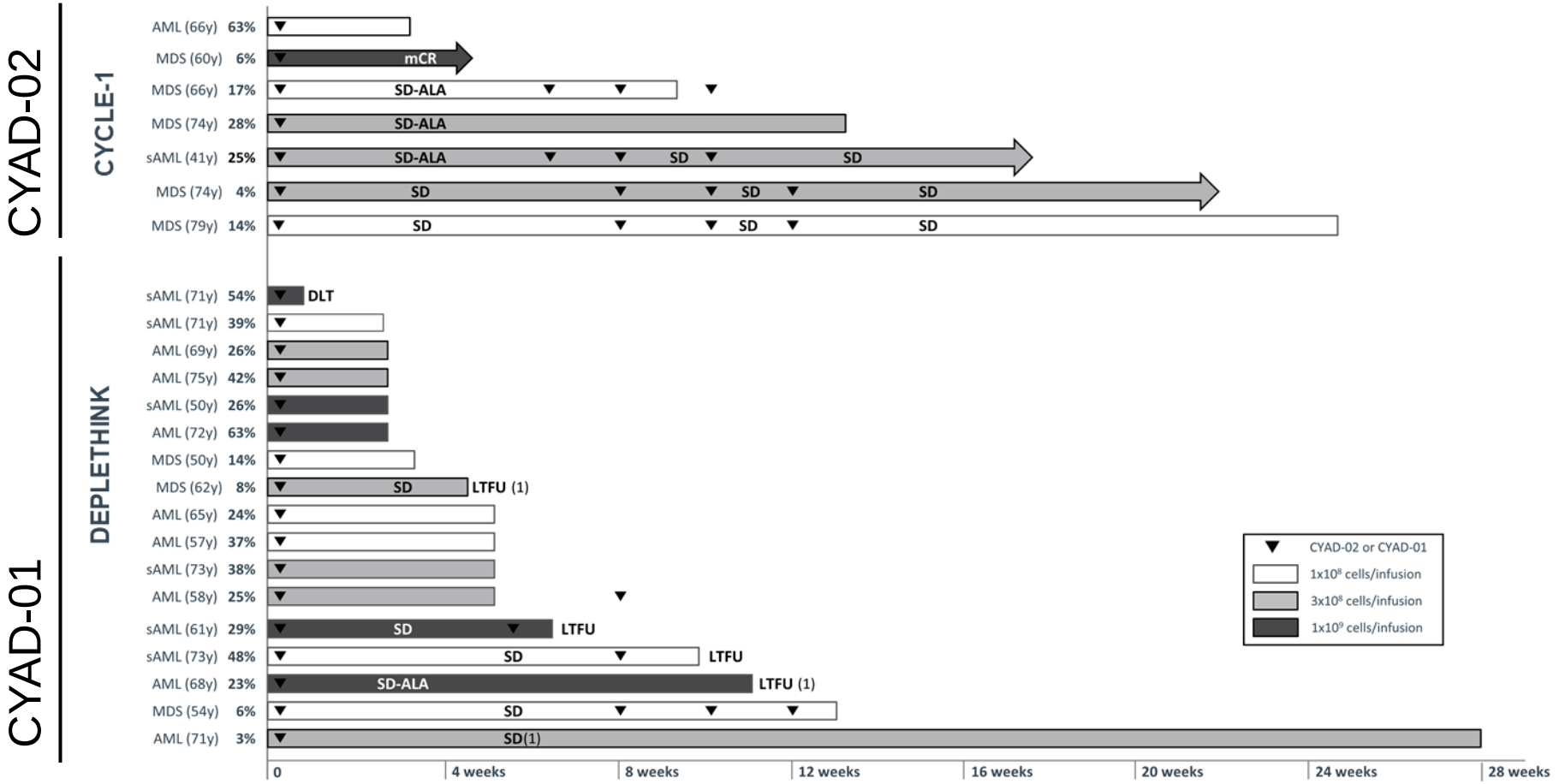
# Preliminary Encouraging Clinical Activity from CYCLE-1 Trial

## Duration of Response




- To date, several patients in CYCLE-1 trial have exhibited a durable stable disease (SD) following treatment of CYAD-02
  - Two very high-risk MDS patients with SD of more than five months (one of two ongoing)
  - One adverse AML patient with SD of four months (ongoing)

Each bar represents one patient. Bar stopped at the first documented progression of the disease or when the patient was lost to follow-up (LTFU). ALA: anti-leukemic activity, defined as a decrease of at least 50% of the bone marrow blasts ; (s)AML: (secondary) acute myeloid leukemia; MDS: myelodysplastic syndrome LTFU: Lost to follow up; SD: Stable disease. (1) Patient not authorized to consolidation cycle due to CYAD-01 peripheral blood persistence

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# CYAD-02 CYCLE-1 – Summary and Next Steps

## Summary of Initial Data

- CYAD-02 generally well-tolerated to date
- Preliminary clinical activity data showed anti-leukemic activity in 50% of r/r AML / MDS patients with an overall encouraging disease control
  - Single patient evaluated at dose level 3 achieved a marrow complete response (mCR) at first assessment (ongoing)
- Two very high-risk MDS patients with SD of more than five months (one of two ongoing)
- One adverse AML patient with SD of four months (ongoing)

## Key Takeaways and Next Steps

- Initial observations of clinical activity observed in the CYCLE-1 study seems attributable to an increased potency of CYAD-02
- Dose level 3 cohort of the CYCLE-1 trial is ongoing
  - Additional safety and activity data from CYCLE-1 trial are expected during the first half of 2021

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AML: Acute myeloid leukemia; MDS: Myelodysplastic syndrome; r/r: relapse/refractory.

# Autologous r/r AML / MDS Program – Next Steps

## First-Generation CYAD-01

- Over 30 r/r AML and MDS patients have been enrolled in the THINK trial across various scenarios, including 8 patients at the $3x10^8$ dose with the OptimAb manufacturing process
- Based on CYAD-01 not achieving our internal thresholds for clinical activity and duration of response in the THINK trial, the company has decided to discontinue the development of CYAD-01 for the treatment of r/r AML / MDS

## Next-Generation CYAD-02

- Dose level 3 cohort of the CYCLE-1 trial is ongoing
  - Additional safety and activity data from CYCLE-1 trial are expected during the first half of 2021

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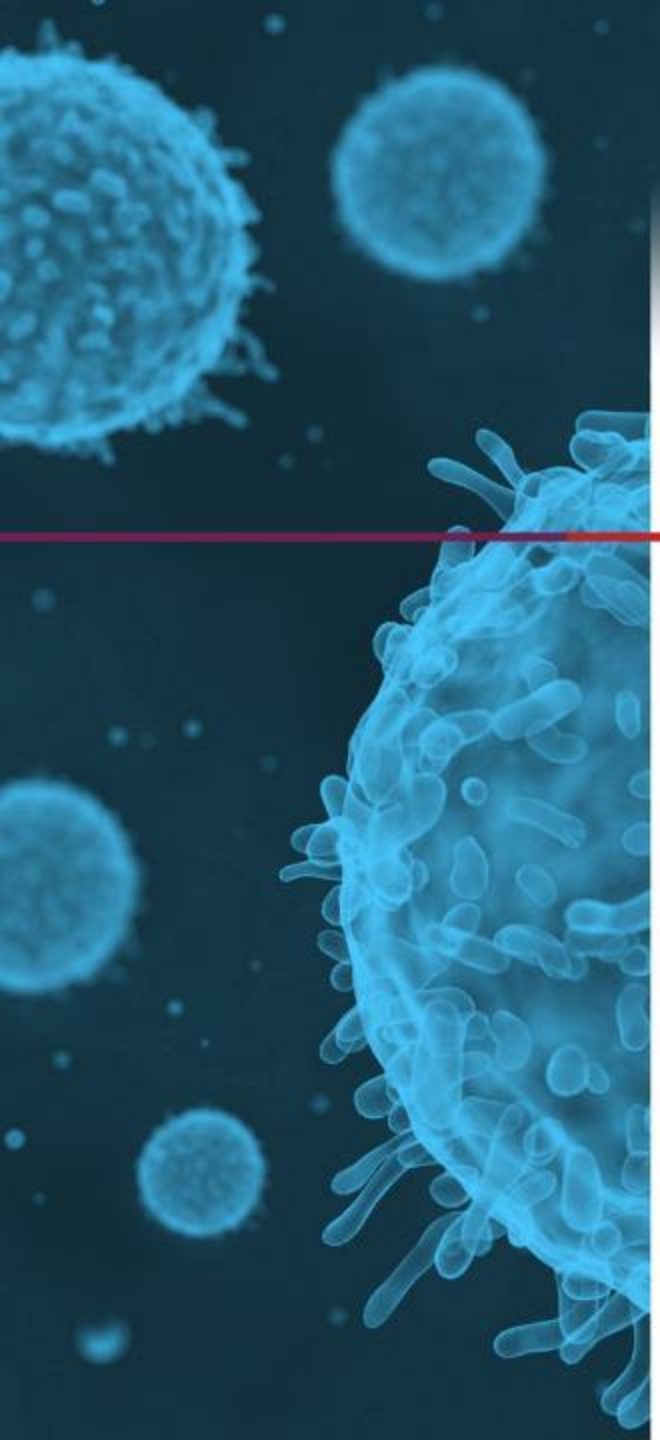
# Upcoming Milestones – Hematological CAR T Pipeline



# Upcoming Anticipated Milestones for Hematological CAR T Pipeline

**CYAD-211**

Report proof-of-concept data on shRNA technology as allogeneic platform from initial dose cohorts of Phase 1 IMMUNICY-1 trial

Report clinical activity data from dose-escalation IMMUNICY-1 trial


**CYAD-02**

Report additional data from CYAD-02 Phase 1 CYCLE-1 trial

- CYAD-211 is the first non-gene edited allogeneic CAR T candidate based on shRNA technology, incorporating a BCMA-targeting scFv and a shRNA targeting the CD3ζ subunit of TCR complex
  - Recruitment ongoing in Phase 1 IMMUNICY-1 trial in r/r MM
- Next-generation, autologous NKG2D receptor-based CYAD-02 uses our shRNA technology, to silence the expression of MICA and MICB with the aim to increase persistence and potency of CAR T cells
  - CYCLE-1 trial ongoing in r/r AML / MDS patients

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