Press Release

Miltenyi Biomedicine presents primary analysis of the pivotal DALY 2-EU trial for second-line relapsed/refractory large B-cell lymphoma at the 67th American Society of Hematology (ASH) Annual Meeting

- ***DALY 2-EU results show zamtocabtagene autoleucel (zamto-cel) demonstrated clinically meaningful superiority over chemoimmunotherapy in patients with relapsed/refractory large B-cell lymphoma (r/r LBCL)[1]***
- ***Zamto-cel was well-tolerated in the majority of patients. DALY 2-EU included a high-risk study population, characterized by older age and clinically high-risk disease features***
- ***A 12-day manufacturing time resulted in a vein-to-vein time of 14-16 days, reducing the likelihood for bridging therapy.***

Bergisch Gladbach, December 7, 2025 – Miltenyi Biomedicine today announced results from the pivotal DALY 2-EU trial evaluating the efficacy and safety of zamtocabtagene autoleucel (zamto-cel) compared with standard chemoimmunotherapy (R-GemOx or Pola-BR) in patients with second-line, relapsed or refractory large B-cell lymphoma (r/r LBCL) who were transplant-ineligible due to age, comorbidities, or other medical reasons.

The primary analysis showed that zamto-cel demonstrated significant and clinically meaningful superiority over chemoimmunotherapy (R-GemOx) in transplant-ineligible patients who were at a high risk of rapid disease progression.[1] This study population was characterized by older age and clinically high-risk disease features: the median age was 74 years, 57% of patients had a high International Prognostic Index (IPI≥ 3) and 67% presented with stage III/IV disease. Zamto-cel was well tolerated in this predominantly older and high-risk population.[1]

Dr. Peter Borchmann, Lead investigator of DALY 2-EU trial and Assistant Medical Director in the Department of Hematology and Oncology at the University Hospital of Cologne, Germany, said: “Zamto-cel demonstrated clinically meaningful and statistically significant superiority over R-GemOx in transplant-ineligible patients with high-risk disease, improving event-free survival while maintaining a favorable tolerability profile. These findings highlight the potential of zamto-cel as an important new treatment option for a clinically vulnerable patient population with limited therapeutic choices.”

Dr. Toon Overstijns, Chief Executive Officer of Miltenyi Biomedicine, said: “The DALY 2-EU results mark an important milestone in our commitment to advancing cell and gene therapies. Zamto-cel - the first tandem CD20-CD19 (directed), non-cryopreserved CAR-T cell therapy - demonstrated meaningful clinical benefit with promising efficacy and safety, bringing us closer to providing much needed treatment options for patients with high-risk lymphomas.”

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- Zamto-cel is the first tandem CD20-CD19 (directed) non-cryopreserved chimeric antigen receptor T (CAR-T) cell therapy. The main mechanisms for relapse after treatments with CD19-directed CAR-T cell therapies are the limited persistence of CAR-T cells, inhibition of CAR-T cell function, and CD19 immunological antigen escape. To minimize the risk of relapse due to CD19 antigen escape, zamto-cel utilizes dual antigen targeting of CD20 and CD19. Zamto-cel has a 12-day manufacturing time, resulting in a vein-to-vein time of 14-16 days and reducing the likelihood for bridging therapy

DALY 2-EU Primary results[1]

At the data cutoff, patients were randomly assigned to receive zamto-cel (n=82) or R-GemOx/ PolaBR (n=86). The trial allowed for crossover, 29 patients received zamto-cel following failure to achieve a response with either R-GemOx (n=28) or Pola-BR (n=1)

Efficacy Results (assessed by the blinded independent review committee (BIRC))

- The median event-free survival (EFS) for zamto-cel was 6.2 months (95% CI 3.8-13.8) compared to 2.5 months (95% CI 2.0-3.3) for R-GemOx (HR 0.39; 95% CI 0.27-0.58; p<0.0001).
- The median progression-free survival (PFS) was significantly longer with zamto-cel at 8.5 months (95% CI 3.8-16.8) versus 3.3 months (95% CI 2.0-3.8) for R-GemOx (HR 0.43 [95% CI 0.28-0.65]; p<0.0001).
- In the intent-to-treat (ITT) population, the overall response rate (ORR) was 72% with a 54% complete response rate (CRR) for zamto-cel compared to 45% ORR and 14% CRR for R-GemOx.

Safety Results[1]

Zamto-cel was well-tolerated in this elderly patient population with high risk

- Grade ≥ 3 cytokine release syndrome (CRS) was reported in 4 patients (5.3).
- Grade 3 Immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in 1 patient (1.3%).

About DALY 2-EU[2]

DALY 2-EU (NCT04844866) is a pivotal, randomized, multi-center, open-label Phase II trial conducted in 12 countries within the EU, evaluating the safety and efficacy of genetically engineered autologous T-cells expressing anti-CD20 and anti-CD19 specific chimeric antigen receptor, zamtocabtagene autoleucel (zamto-cel), compared to chemoimmunotherapy (CIT), (rituximab, gemcitabine, and oxaliplatin (R.GemOx)) or polatuzumab vedotin plus bendamustine/rituximab (Pola-BR)), as a second-line therapy for primary relapsed/refractory large B-cell lymphoma (r/r LBCL). To our knowledge, is the only CAR-T randomized study in this patient population to date.

Eligible patients were adults with r/r LBCL who were refractory or relapsed within 24 months from the start of their first-line treatment, had received at least an anthracycline and a rituximab-containing regimen and were ineligible for a stem-cell transplant.

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Participants were randomized 1:1 to receive either zamto-cel or CIT (R-GemOx/Pola-BR). Zamto-cel was administered as a single non-cryopreserved infusion at a dose of 2.5 x 10^6 CAR-transduced T cells per kg body weight after lymphodepletion with fludarabine and cyclophosphamide. Patients randomized to the comparator arm received either R-GemOx or Pola-BR.

The primary endpoint of the trial is event-free survival (EFS) assessed by a blinded independent review committee (BIRC), defined as the time from randomization to objective disease progression, failure to achieve a partial response (PR) or complete response (CR) at or beyond Week 8, leading to a new anti-lymphoma therapy or death from any cause. Secondary endpoints include progression-free survival (PFS), best complete response rate (CRR), duration of complete response (DOR), and overall survival (OS).

These data will be reported as part of a pre-planned EFS interim analysis after a median follow-up of 17 months. Additional analyses are planned with longer follow-up periods and will be presented at future meetings.

DALY 2-EU results join previous zamto-cel publications in other indications and populations, including:

- DALY II USA (NCT04792489), a multicenter, open label, single-arm Phase II trial of zamto-cel in patients with r/r DLBCL after at least two prior lines of treatment, including anti-CD20 monoclonal antibody and anthracycline-containing regimen and measurable disease per Lugano 2014 classification. The ORR in the evaluable patient population (n=59) as assessed by an Independent Radiology Committee was 72.9% (95% CI, 59.7-83.6) with a CRR of 49.2% (95% CI, 35.9-62.5).
- In the DALY II USA clinical trial, a dedicated cohort for r/r central nervous system lymphoma was opened. In this cohort of 16 patients, the data showed an overall response rate of 80% and 100% and a complete response rate of 50% and 100% in the PCNSL (primary CNS lymphoma) and SCNSL (secondary CNS lymphoma) respectively.
- Zamto-cel is being explored in r/r Mantle cell lymphoma (MCL) and r/r Richter's transformation (RT)

About zamtocabtagene autoleucel (zamto-cel)
Zamto-cel is an investigational autologous chimeric antigen receptor (CAR) T-cell therapy designed to target both CD20 and CD19. It is being studied in clinical trials for the treatment of relapsed or refractory B-cell malignancies, including large B-cell lymphoma (LBCL), diffuse large B-cell lymphoma (DLBCL), primary and secondary central nervous system (CNS) lymphoma, mantle cell lymphoma (MCL), Richter's transformation (RT), and other B-cell neoplasms.

Zamto-cel is manufactured using Miltenyi's proprietary platform, a closed, automated system. The manufacturing time of 12 days results in a vein-to-vein time of 14-16 days,

reducing the need for bridging therapy and increasing the ability to receive cellular therapy for high risk patients with urgent therapeutic needs. Its non-cryopreserved formulation eliminates cryopreservation-related logistical steps and costs.

About Miltenyi Biomedicine
Miltenyi Biomedicine is committed to making innovative cancer treatments and regenerative therapies accessible to patients with serious diseases. Leveraging cutting-edge technology, the company innovates independently to address hard-to-treat blood cancers and harness the potential of CAR technology to transform patient care. Miltenyi Biomedicine is currently investigating its first cell therapy asset.

About Miltenyi Biotec
Miltenyi Biotec is a global leader in innovating technologies and services for patient-specific cell and gene therapies, transforming scientific discoveries into practical treatments for personalized medicine. With over 35 years of expertise, it supports biomedical discoveries and translates them into clinical applications, enhancing patient access to new therapies. Miltenyi Biotec, with its integrated solutions, including GMP-certified cell factories, provides expert guidance to therapy developers efficiently from process development to commercialization through its Miltenyi Bioindustry global CDMO division.

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