# ICD-10-PCS Procedure Code Request for Administration of Obecabtagene Autoleucel

ICD-10 Coordination & Maintenance Committee Meeting

March 2024

# Legal Notices

- *These slides are directed to the audience of this presentation for the sole purpose of supporting the request for an ICD-10-PCS procedure code for obecabtagene autoleucel.*
- *Autolus's products and therapies are investigational; they have not been approved by any regulatory authority, including the FDA. The safety and efficacy of Autolus's investigational products and therapies has not been established. Nothing in this presentation should be taken to be any form of promotion or advertisement of any of Autolus's investigational products or therapies.*
- *All statements contained herein should be taken in the context of providing educational information and data from Autolus's investigational trials to health care professionals who: (1) Are affiliated with institutions currently involved in Autolus sponsored or collaborative research; (2) Are affiliated with institutions currently under CDA with the intent to operationalize cell therapy in the event obe-cel is approved by the FDA; and/or (3) Have requested updates on the Autolus clinical development program.*
- *As a regulatory requirement in connection with our Biologics License Application (BLA) at the FDA, Autolus is required to assess, qualify, and monitor each treatment center for the center's ability to deliver CAR-T cell therapy.*
- *Please always refer to the final, approved labelling for full information about the product (including administration of the product), if and when it becomes available.*

# High unmet treatment need for adult patients with R/R ALL

Successful therapy requires high level of activity and sustained persistence paired with good tolerability

- Median overall survival is < 1 year in adult R/R ALL; highest rate of death among people 65-74 years of age[1]
- Combination chemotherapy enables 90% of newly diagnosed adult ALL patients to experience Complete Response (CR); only 30% to 40% achieve long-term remission[2,3]
- Current T-cell therapies for adult patients with R/R ALL are highly active, with poor tolerability, limited persistence of CAR T-cell activity and frequently followed by subsequent treatment (e.g., allo-SCT)[4-6]
  - Current CAR T-cell therapy induces increased rates of severe CRS and high rates of severe ICANS
- Older ALL patients, those with high tumor burden, or those in overall poor health may not be eligible to receive current treatment options
  - Allo-SCT, as they may not be able to tolerate pre-transplant conditioning therapy
  - CAR T therapies, because of treatment-related toxicities

ALL, acute lymphoblastic leukemia; allo-SCT, allogeneic stem cell transplant; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; R/R, relapsed/refractory

1. SEER, accessed October 2023; 2. American Cancer Society, 2021; 3. Sheykhhasan M, et al. *Cancer Gene Ther* 2022; 4. Kantarjian H, et al. *N Engl J Med* 2017; 5. Hadjivassileva T, et al. EBMT-EHA 2023; 6. Shah BD, et al. *Lancet* 2021.

# Obe-cel background – a fast-off CD19 CAR T therapy

- CD19 CAR-T therapy has revolutionized the field of R/R B-ALL[1]
- Obe-cel is an autologous CD19 CAR with a proprietary fast off-rate CD19 binding domain designed to mitigate safety concerns and improve persistence[2,3]
- The clinical activity of obe-cel has been tested in pediatric[2] and adult R/R B-ALL[3], and more recently in other B-cell malignancies (NCT02935257)[4]
- The Biologics License Application (BLA) for obe-cel was submitted to the FDA on November 27, 2023
- Earlier, the FDA granted obe-cel Orphan Drug Designation and Regenerative Medicine Advanced Therapy (RMAT) Designation

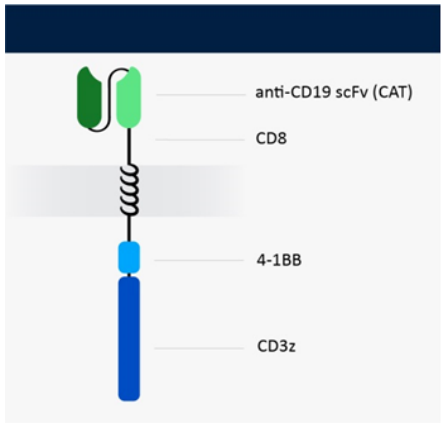
**ASCO 2023: Results from adult patients with R/R B-ALL treated with obe-cel in the pivotal FELIX Phase II study (NCT04404660)[5]**

B-ALL, B-cell precursor acute lymphoblastic leukemia; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; R/R, relapsed/refractory

1. Pasvolsky O, et al. *Blood Adv* 2023; 2. Ghorashian S, et al, *Nat Med* 2019; 3. Roddie C, et al, J *ClinOncol* 2021; 4. Roddie C, et al. *Blood* 2022; 5. Roddie C, et al. J Clin Oncol 2023.

# Obe-cel has a unique mechanism of action

Designed for increased activity and reduced toxicity




Proprietary CD19 binder with fast off-rate

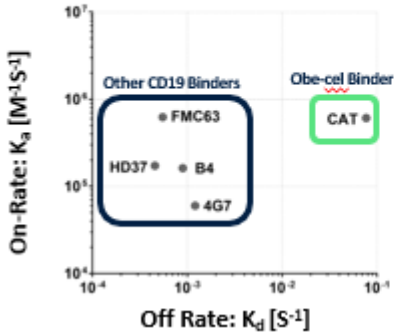
## Potential for improved potency, reduced toxicity

Avoided over-activation of CAR T cells
-> Reduced toxicities

Increased CAR T peak expansion
-> Improved persistence

Avoided exhaustion of CAR T cells
-> Improved engraftment
-> Improved persistence

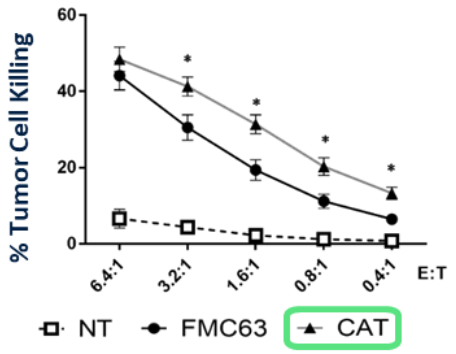
## Fast off-rate

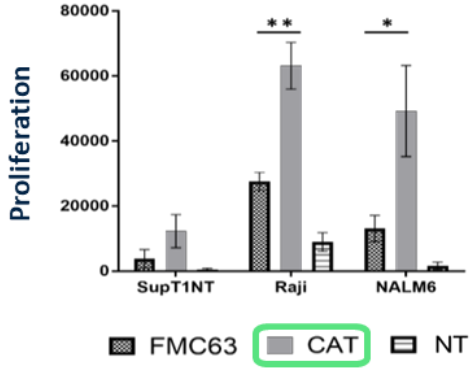



Obe-cel has a shorter half-life of interaction compared to FMC63 binder used in other approved products

- obe-cel = 9.8 seconds
- FMC63 = 21 minutes

## Enhanced cytotoxicity and proliferation

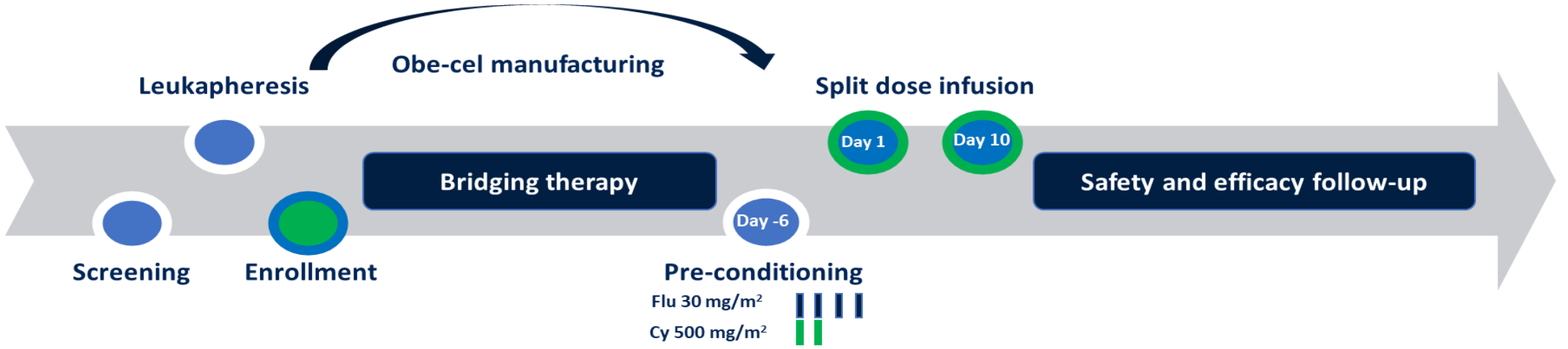



Ghorashian et al. Nature Medicine 2019

# Treatment Journey: obe-cel for adults with R/R B-ALL

(First-In-Class Tumor Burden Guided Dosing)





**94% of infused patients received both obe-cel infusions**

B-ALL, B-cell precursor acute lymphoblastic leukemia; R/R, relapsed/refractory.

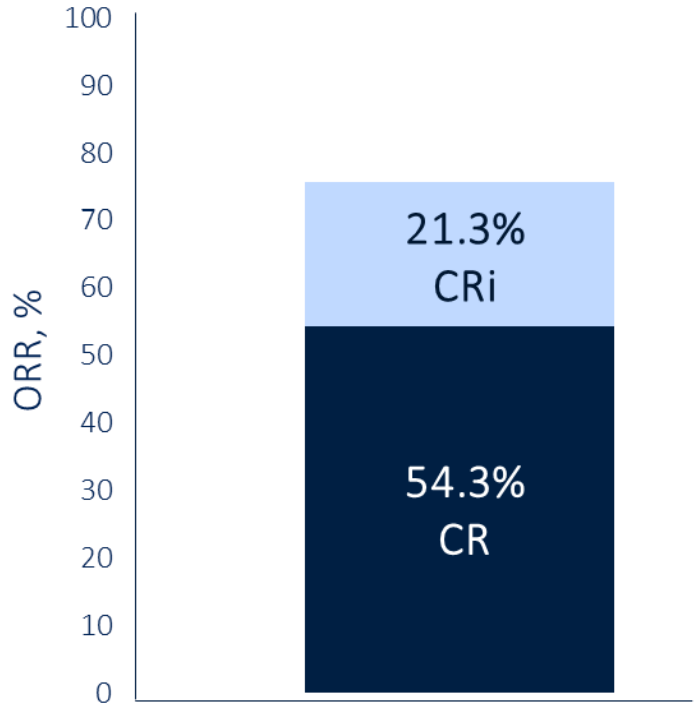
# Administration of obe-cel

There is no ICD-10-PCS code that identifies the intravenous administration of obe-cel

- **How supplied:** Obe-cel is supplied as a cryopreserved autologous cell suspension packaged in three or more infusion bags overall containing a cell dispersion of the **target dose of 410 x $10^6$ CD19 CAR-positive viable T cells**:
  - 10 x $10^6$ CAR-positive viable T cells in one 50 mL bag
  - 100 x $10^6$ CAR-positive viable T cells in one or more 50 mL or 250 mL bags
  - 300 x $10^6$ CAR-positive viable T cells in one or more 250 mL bags
- **Tumor burden guided dosing (Day 1 and Day 10):** Personalized to each patient according to their bone marrow disease burden; designed to minimize treatment toxicity related to tumor burden
  - If the patient has <20% bone marrow blasts, the Day 1 dose is 100 x $10^6$ CAR T cells; the second dose (Day 10) is 310 x $10^6$ CAR T cells
  - If the patient's tumor burden is >20% bone marrow blasts, the Day 1 dose is 10 x $10^6$ CAR T cells and the second dose (Day 10) is 400 x $10^6$ CAR T cells
  - Patients with Grade 2 CRS and/or Grade 1 ICANS following the first dose may receive the second dose on Day 10 ($\pm$2 days) only if CRS has resolved to Grade 1 or less and ICANS has completely resolved
- **Storage / handling / administration:** Obe-cel will be shipped and stored in vapor-phase liquid nitrogen containers (below -150$^o$C) and will be thawed in a 37$^o$C water bath under sterile conditions prior to administration via intravenous infusion over a few minutes (maximum 30 minutes from obe-cel being thawed to preserve cell viability)
- It is expected that the obe-cel infusion procedure will be documented in the medical record in the same manner as other cellular therapies that are administered via intravenous infusion

# Disease Response per IRRC Assessment

76% of infused patients achieved CR/CRi



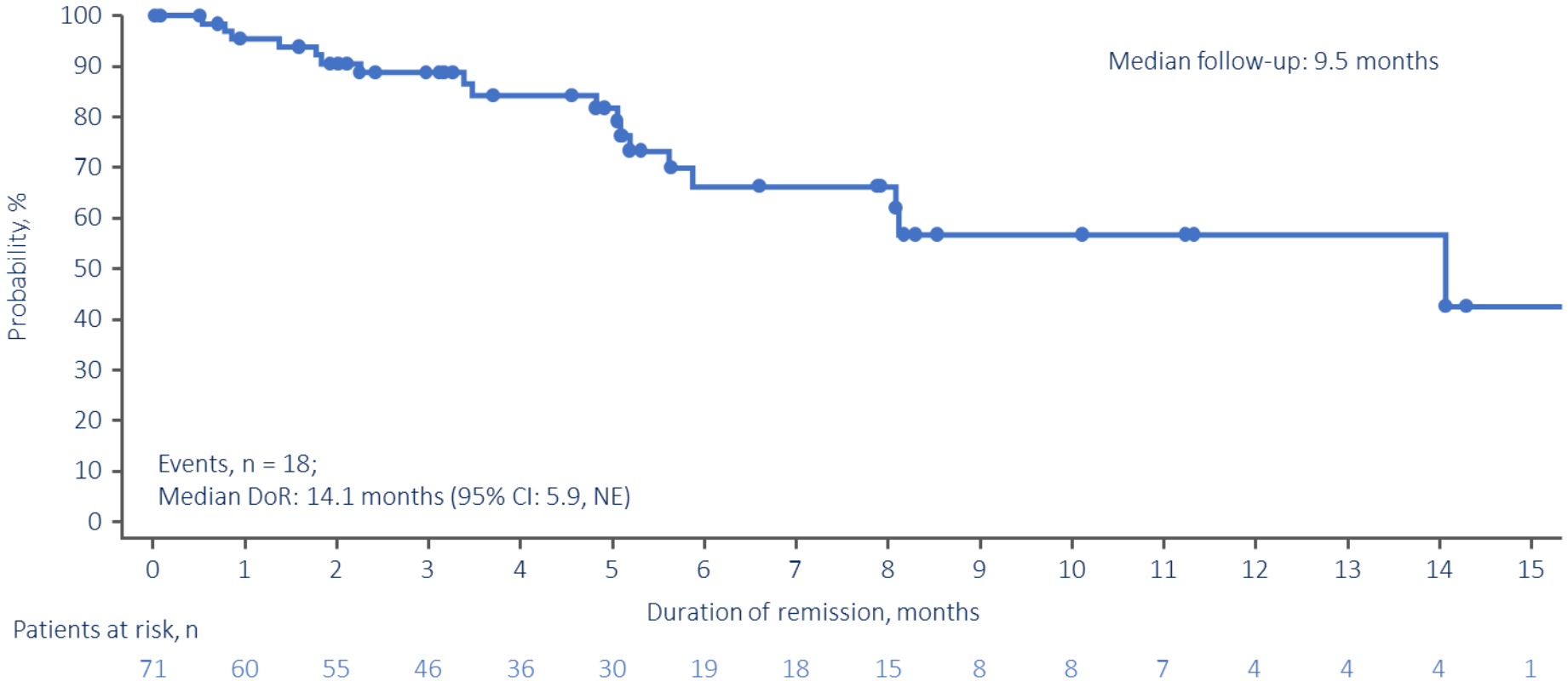

**ORR: 76%**
95% CI (66, 84)
p<0.0001*

**97% of responders with evaluable samples were MRD negative at $10^{-4}$ level by flow cytometry**

*One-sided p-value from the exact test on H0: ORR ≤40% vs H1: ORR >40%
CR, complete remission, CRi, CR with incomplete blood count recovery; IRRC, independent response review committee; MRD, minimal residual disease; ORR, overall remission rate

# FELIX: duration of remission

61% responders in ongoing remission without subsequent anti-cancer therapies




**13% responders who proceeded to SCT while in remission were censored at the time of SCT**

NE, not estimable

# FELIX: safety – TEAEs

| TEAEs that occurred in ≥20% of patients regardless of causality | All infused patients (N=94) | |
|---|---|---|
| | Any grade, % | Grade ≥3, % |
| Patients with any TEAE | 98.9 | 78.7 |
| CRS | 75.5 | 3.2 |
| Neutropenia/neutrophil count decreased | 39.4 | 36.2 |
| Thrombocytopenia/platelet count decreased | 28.7 | 25.5 |
| Nausea | 28.7 | 1.1 |
| Pyrexia | 27.7 | 1.1 |
| Febrile neutropenia | 25.5 | 25.5 |
| Headache | 25.5 | 0 |
| ICANS | 25.5 | 7.4 |
| Diarrhea | 24.5 | 0 |
| Anemia | 22.3 | 19.1 |
| Hypotension | 20.2 | 4.3 |

- The most common Grade ≥3 TEAEs were neutropenia (36.2%), thrombocytopenia (25.5%), febrile neutropenia (25.5%), and anemia (19.1%)
- One death (1/94; 1%) was considered obe-cel-related per investigator assessment (HLH and neutropenic sepsis)

CRS, cytokine release syndrome; HLH, hemophagocytic lymphohistiocytosis; ICANS, immune effector cell-associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event

# FELIX: safety – CRS and ICANS

Low rates of Grade ≥3 CRS and/or ICANS were observed

| | BM blasts ≤20% at pre-conditioning (N = 37) | BM blasts >20% at pre-conditioning (N = 57) | All infused patients (N = 94) |
|---|---|---|---|
| CRS | | | |
| Any grade, n (%) | 24 (64.9) | 47 (82.5) | 71 (75.5) |
| Grade ≥3, n (%) | 1 (2.7) | 2 (3.5) | 3 (3.2) |
| ICANS | | | |
| Any grade, n (%) | 5 (13.5) | 19 (33.3) | 24 (25.5) |
| Grade ≥3, n (%) | 1 (2.7) | 6 (10.5) | 7 (7.4) |

- Tocilizumab and steroid was used to treat CRS in 53/94 (56%) and 16/94 (17%) patients, respectively
- 3/94 (3%) patients required vasopressor for treatment of CRS
- 6/7 (86%) Grade ≥3 ICANS were observed among patients with >75% BM blasts at pre-conditioning

BM, bone marrow; CRS, cytokine release syndrome; ICANS, immune effector cell associated neurotoxicity syndrome

# Obe-cel is designed to address the high unmet treatment need in adult R/R B-ALL

- For adults with R/R B-ALL, new treatment options are needed to achieve high response rates and long-term remissions, with manageable safety and an improved patient journey
- The pivotal FELIX population represents the largest (N=94) and most diverse patient population studied for adult R/R B-ALL with CAR T therapy, including a strong representation of Medicare-eligible patients
  - 48 of the 94 patients were 50 years of age or older, with 21 over 65 years of age
  - Patients were heavily pre-treated with high disease burden at study entry; 30.9% had ≥3 prior lines of therapy
  - 30% of patients identified as Hispanic, a population with a higher B-ALL prevalence rate
- Obe-cel infusion resulted in a CR/CRi rate of 76%; with a median of 9.5 months' follow-up, 61% of responders remain in remission
  - In the earlier Phase 1 study, 35% of patients (7/20) had ongoing remission without any consolidation therapy ≥2 years after obe-cel treatment (36-month median follow-up)[1]
- Obe-cel infusion resulted in very low rates of Grade ≥3 CRS (3.2%) and low rates of Grade ≥3 ICANS (7.4%)
  - This compares favorably to rates reported with current T cell therapies
- These data suggest that obe-cel has the potential for long-term clinical benefit for adult patients with R/R B-ALL patients without additional therapies

B-ALL, B-cell precursor acute lymphoblastic leukemia; R/R, relapsed/refractory

1. Roddie C, et al. *Blood* 2022 [presented at ASH 2022]