# OBX-115 engineered tumor-infiltrating lymphocyte (TIL) cell therapy with regulatable membrane-bound IL15 (mbIL15) in patients with advanced melanoma that has progressed on/after immune checkpoint inhibitors

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# Key Takeaways

1

The OBX-115 **safety** profile is differentiated by exclusively **low-dose lymphodepletion** and **absence of IL2**

2

Promising early **efficacy** was observed, with a **67% ORR** and potential for **durable** and **deepening** responses

3

Key **regimen benefits** may provide a meaningful treatment option to a **broader patient population**

IL2, interleukin 2; ORR, objective response rate.

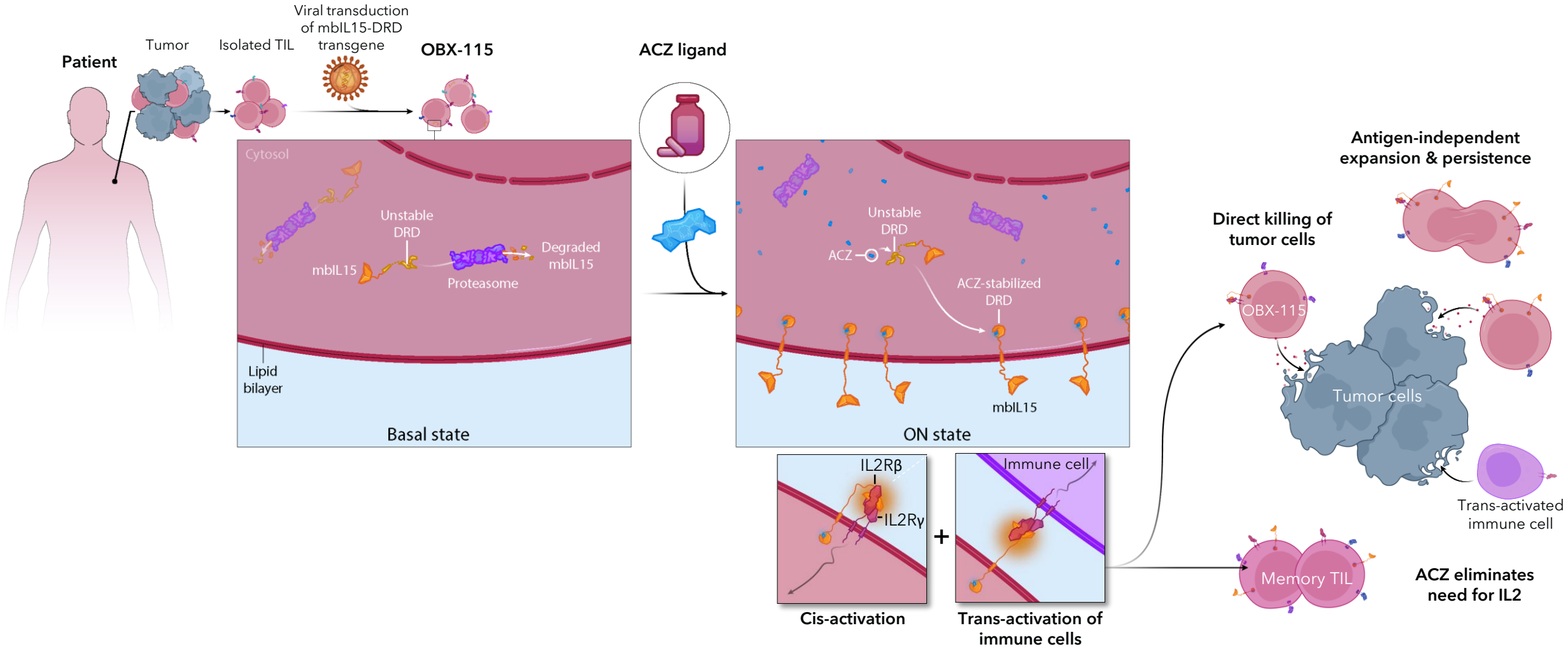
# Background

- OBX-115 engineered TIL cell therapy expresses regulatable **membrane-bound interleukin 15** (**mbIL15**) via administration of the small-molecule drug **acetazolamide** (**ACZ**)
- OBX-115 offers several clinical advantages over conventional non-engineered tumor-infiltrating lymphocyte (TIL) cell therapy:
  - Option for less-invasive tumor tissue procurement (TTP) by **core needle biopsy**
  - Exclusively **low-dose lymphodepletion** compatible with **outpatient** administration
  - **ACZ-driven mbIL15** expression
  - **Regulatable** and **reinducible** TIL expansion and persistence
- Early clinical data demonstrated **differentiated safety** and **promising efficacy** at the recommended phase 2 dose (RP2D)[1]
- We report data from additional patients evaluating OBX-115 at the RP2D in patients with advanced melanoma treated in the Agni-01 study

1. Chesney JA et al. ASCO 2025 (Abstract 9517).
ACZ, acetazolamide; mbIL15, membrane-bound interleukin 15; RP2D, recommended phase 2 dose; TIL, tumor-infiltrating lymphocytes; TTP, tumor tissue procurement.

# OBX-115 Mechanism of Action

## ACZ-regulated mbIL15 activates OBX-115 and other immune cells




ACZ, acetazolamide; DRD, drug-responsive domain; IL2, interleukin 2; mbIL15, membrane-bound interleukin 15; TIL, tumor-infiltrating lymphocytes.



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# Agni-01 Single-arm Open-label Phase 1/2 Study

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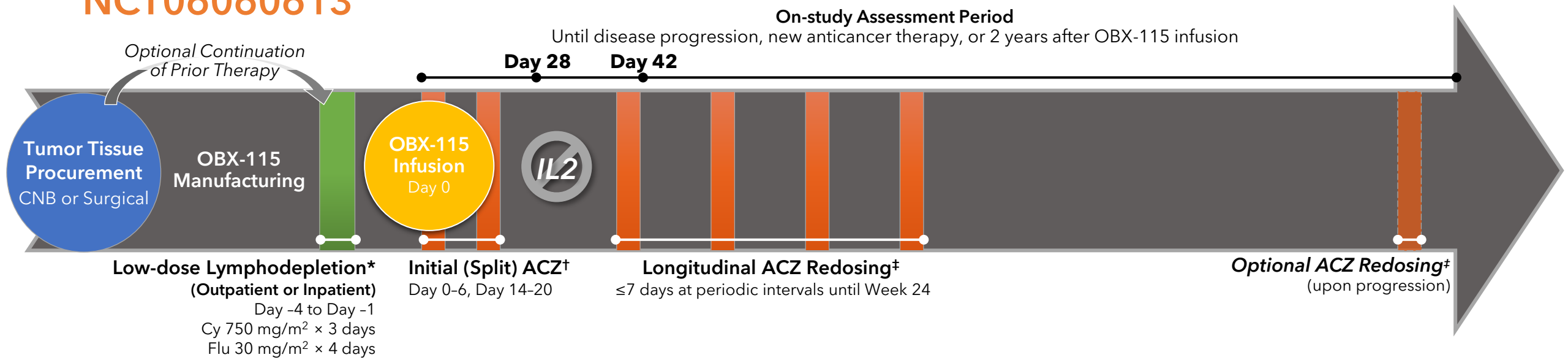


### Treatment Regimen

- **Low-dose lymphodepletion**
- **OBX-115**: 1–100 ×$10^9$ cells
  **ACZ:** 500 mg/day orally
  - **Initial split-dose ACZ**†
  - **Longitudinal ACZ redosing**‡ after recovery from lymphodepletion

### Key Eligibility Criteria

- Advanced non-uveal melanoma progressing after ICI therapy
- No upper age limit
- Not restricted by LDH, HLA, or melanoma subtype
- ≥1 lesion suitable for TTP for manufacturing and ≥1 remaining lesion amenable to RECIST v1.1 response assessment
  - **Minimally invasive TTP (core needle biopsy)** feasible

Data cutoff: 22 January 2026. *May be administered in the outpatient or inpatient setting, per institutional standard. †Initial ACZ dosing was split into two ≤7-day periods within 28 days (Day 0–6 or until ALC ≥5000 cells/μL, whichever is earlier, and restarting between Day 14 and 21). ‡Longitudinal ACZ redosing for ≤7 days at periodic intervals until Week 24, and upon progression when new anticancer therapy is not immediately warranted.
ACZ, acetazolamide; CNB, core needle biopsy; Cy, cyclophosphamide; Flu, fludarabine; HLA, human leukocyte antigen; ICI, immune checkpoint inhibitor; IL2, interleukin 2; LDH, lactate dehydrogenase; RECIST, Response Evaluation Criteria in Solid Tumors; TTP, tumor tissue procurement.



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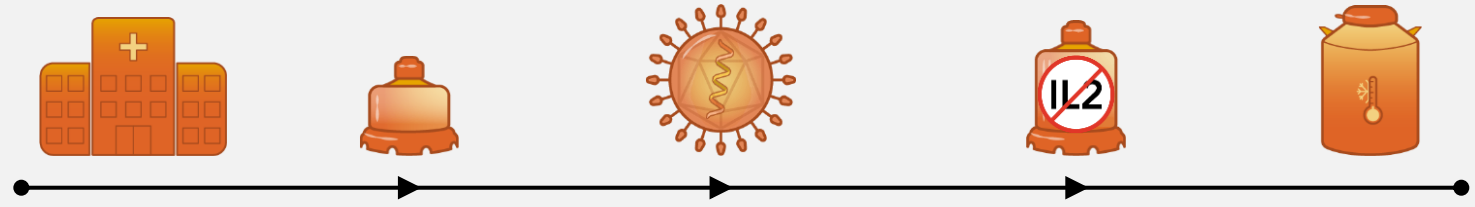
# OBX-115 Differentiated Manufacturing Process

## Designed to achieve a CD8+ enriched and non-exhausted infusion product

### Ex Vivo Manufacturing




**Tumor tissue procurement**
Compatible with core needle biopsy

**Optimized pre-REP**
**Anti-4-1BB** agonist antibody

**Activation / mbIL15 transduction**
Anti-CD3 Ab
Retroviral vector

**Optimized REP**
**iFeeder** cells expressing **IL21** and **4-1BBL**
**ACZ** (**no IL2**)

**Cryo-preservation**

Median (range) infused dose:
**83.4 (34.2–100) ×10⁹ cells***

| Median (range), % | OBX-115 N=15 |
|---|---|
| **CD8+ T cells†** | **97.8 (83.6–99.7)** |
| CD4+ T cells† | 0.2 (Not detected–1.1) |
| NK cells† | 0.3 (Not detected–14.9) |
| PD-1‡ | 0.4 (0.1–2.6) |

Data cutoff: 22 January 2026. *Infused dose was limited to protocol-specified maximum of 100 ×10⁹ cells. †Of all live cells. ‡Of all CD3+CD8+ cells.
4-1BBL, 4-1BB ligand; Ab, antibody; ACZ, acetazolamide; IL2, interleukin 2; IL21, interleukin 21; mbIL15, membrane-bound interleukin 15; NK, natural killer; PD-1, programmed cell death protein 1; REP, rapid expansion protocol.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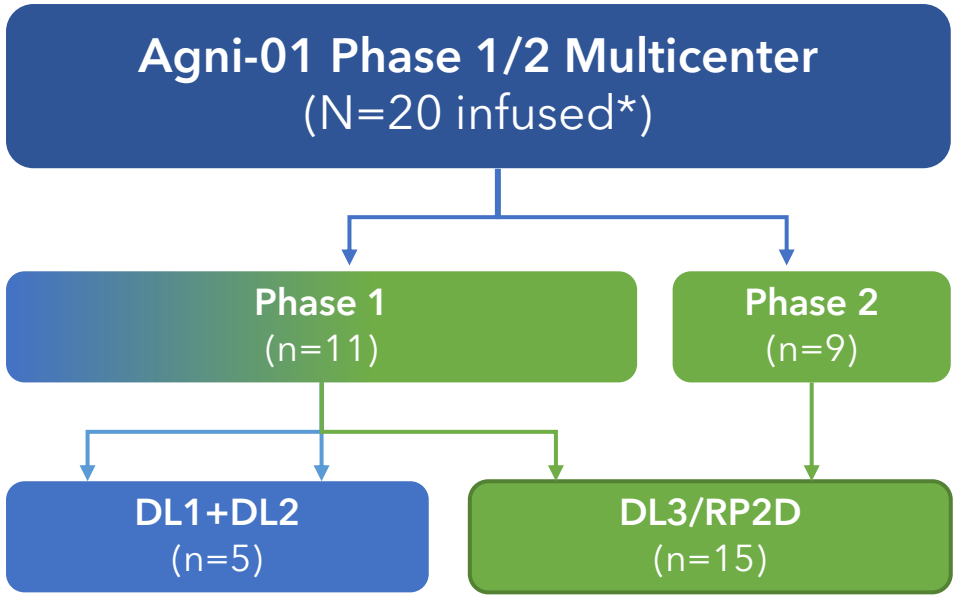
# 15 Patients Treated with OBX-115 at DL3 / RP2D




| | DL1 | DL2 | DL3/RP2D |
|---|---|---|---|
| **OBX-115** | 30 × $10^9$ cell maximum (n=3) | 100 × $10^9$ cell maximum (n=2) | 100 × $10^9$ cell maximum (n=15) |
| **ACZ** | 250 mg/day, Days 0–13 | 250 mg/day, Days 0–13 | 500 mg/day, Days 0–6, 14–20 |

**At DL3/RP2D:**

**4** outpatient lymphodepletion

**100%** of ACZ redosing in outpatient setting†

Data cutoff: 22 January 2026. *3 additional patients were enrolled and not infused: n=2 discontinued prior to treatment due to disease progression during DLT stagger phase; n=1 manufacturing failure. †14 patients received ACZ redosing, all of which were done in the outpatient setting.
ACZ, acetazolamide; DL, dose level; RP2D, recommended phase 2 dose.

# Patients Had Difficult-to-treat ICI-refractory Advanced Melanoma

## 93% with prior anti–PD-1 combination exposure

| Baseline Patient and Disease Characteristics | OBX-115 (N=15) |
|---|---|
| Age, median (range), years | 55 (41–78) |
| Sex, n (%)<br>Female | 6 (40.0) |
| ECOG PS, n (%)<br>0<br>1 | <br>12 (80.0)<br>3 (20.0) |
| LDH >ULN, n (%) | 6 (40.0) |
| Melanoma subtype, n (%)<br>Cutaneous<br>**Mucosal**<br>**Acral** | <br>9 (60.0)<br>**3 (20.0)**<br>**3 (20.0)** |
| Mutation status, n (%)<br>*BRAF* V600-mutant<br>*NRAS*-mutant | <br>8 (53.3)<br>3 (20.0) |
| **Brain and/or liver lesions, n (%)** | **3 (20.0)** |
| Target lesion SOD, mean (SD), mm | 58.0 (14.2–213.0) |

| Treatment Characteristics | OBX-115 (N=15) |
|---|---|
| Lines of prior systemic therapy, median (range)*<br>**Lines of prior ICI therapy** | 2.0 (1–5)<br>**2.0 (1–5)** |
| Prior systemic therapy, n (%)<br>Anti–PD-1 monotherapy only<br>**Anti–PD-1 combination**<br>**Anti–PD-1 + anti–CTLA-4**<br>Anti–PD-1 + anti-LAG3<br>**BRAF ± MEK TKI** | 15 (100.0)<br>1 (6.7)<br>**14 (93.3)**<br>**11 (73.3)**<br>8 (53.3)<br>**6/8 (75.0)** |
| **Primary-resistant (SITC criteria), n (%)**<br>Anti–PD-1[1]<br>Anti–PD-1 combination[2] | **11/15 (73.3)**<br>5/9 (55.6)<br>8/14 (57.1) |

- Patients had advanced and difficult-to-treat disease
- Disease progressed on several lines of standard-of-care therapies
  - **73% with prior anti–PD-1 + anti–CTLA-4 combination**
- Limited remaining treatment options

Data cutoff: 22 January 2026. *Multiple prior lines were permitted.

**1**. Kluger HM et al. *J Immunother Cancer* 2020;8(1). **2**. Kluger H et al. *J Immunother Cancer* 2023;11(3).

CTLA-4, cytotoxic T-lymphocyte antigen-4; ECOG PS, Eastern Cooperative Oncology Group performance status; ICI, immune checkpoint inhibitor; LAG3, lymphocyte activation gene 3; LDH, lactate dehydrogenase; PD-1, programmed cell death protein-1; SITC, Society for Immunotherapy of Cancer; SOD, sum of diameters; TKI, tyrosine kinase inhibitor; ULN, upper limit of normal.



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# Strong Early Efficacy in 2L+ Advanced Melanoma

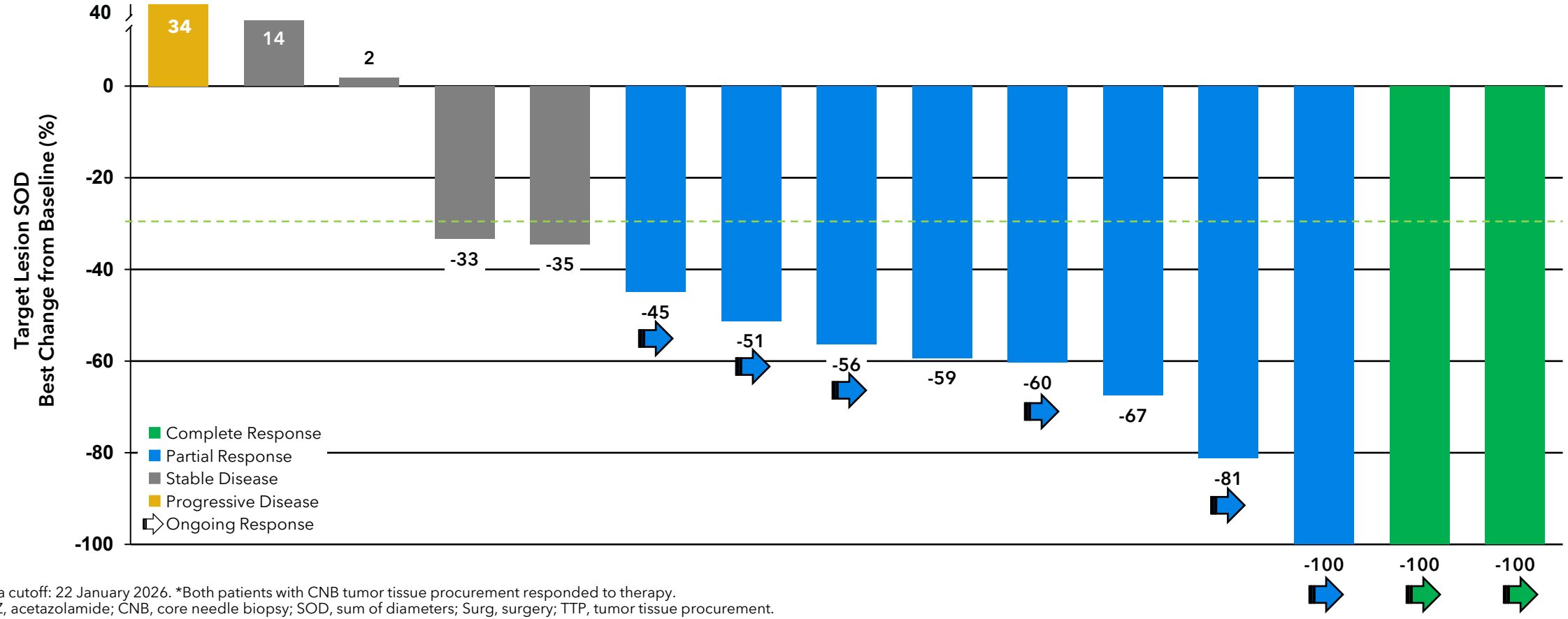
| | OBX-115 (N=15) |
|---|---|
| **Objective response rate, n (%)** | **10 (67)*** |
| Complete response | 2 (13) |
| Partial response | 8 (53) |
| Stable disease | 4 (27) |
| Progressive disease | 1 (7) |
| Disease control rate,† n (%) | 13 (93) |
| **Duration of response, months (median [range])** | **NR (1.1+, 14.9+)** |

- Median (range) study follow-up: 4.3 months (2.3–16.9)
- **Encouraging efficacy**
- Early data suggest **durability of responses**

Data cutoff: 22 January 2026. *95% CI: 38%, 88%. †Disease control rate defined as patients whose best overall response was documented as CR, PR, or SD per RECIST 1.1 criteria, provided that the minimum duration of SD was maintained for ≥12 weeks (N=14).
2L, second-line; NR, not reached.

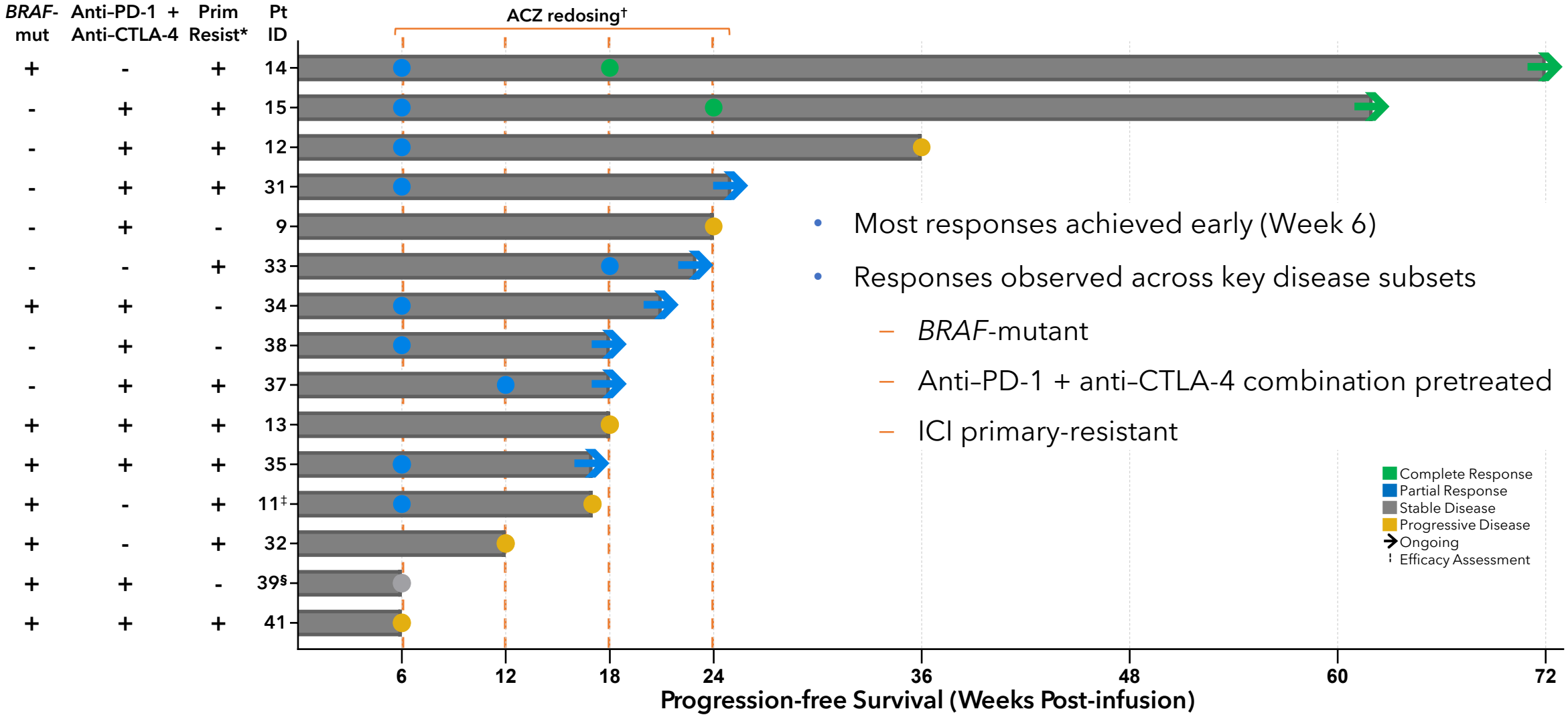
# 67% ORR, with SOD Reduction in 80% of Patients

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **TTP method** | Surg | Surg | Surg | Surg | Surg | **CNB*** | Surg | Surg | Surg | **CNB*** | Surg | Surg | Surg | Surg | Surg |
| **OBX-115 dose (cells × $10^9$)** | 94.8 | 100 | 55.8 | 60.9 | 34.2 | 99.2 | 81.6 | 37.2 | 77.4 | 100 | 86 | 83.4 | 89.2 | 65.7 | 97.6 |
| **ACZ redosing** | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + |
| **Patient ID** | **41** | **39** | **13** | **32** | **9** | **33** | **35** | **34** | **12** | **31** | **11** | **38** | **37** | **15** | **14** |




Data cutoff: 22 January 2026. *Both patients with CNB tumor tissue procurement responded to therapy.
ACZ, acetazolamide; CNB, core needle biopsy; SOD, sum of diameters; Surg, surgery; TTP, tumor tissue procurement.

# Onset and Duration of Responses




- Most responses achieved early (Week 6)
- Responses observed across key disease subsets
  - *BRAF*-mutant
  - Anti–PD-1 + anti–CTLA-4 combination pretreated
  - ICI primary-resistant

Data cutoff: 22 January 2026. *ICI primary-resistant disease (monotherapy or combination therapy). †ACZ was redosed after recovery from lymphodepletion for 7 days every 6 weeks until Week 24. ‡Patient 11 did not receive combination anti–PD-1 therapy. §Patient 39 censored prior to Week 12.
ACZ, acetazolamide; CTLA-4, cytotoxic T-lymphocyte antigen-4; ICI, immune checkpoint inhibitor; mut, mutant; PD-1, programmed cell death protein-1; prim resist, primary-resistant.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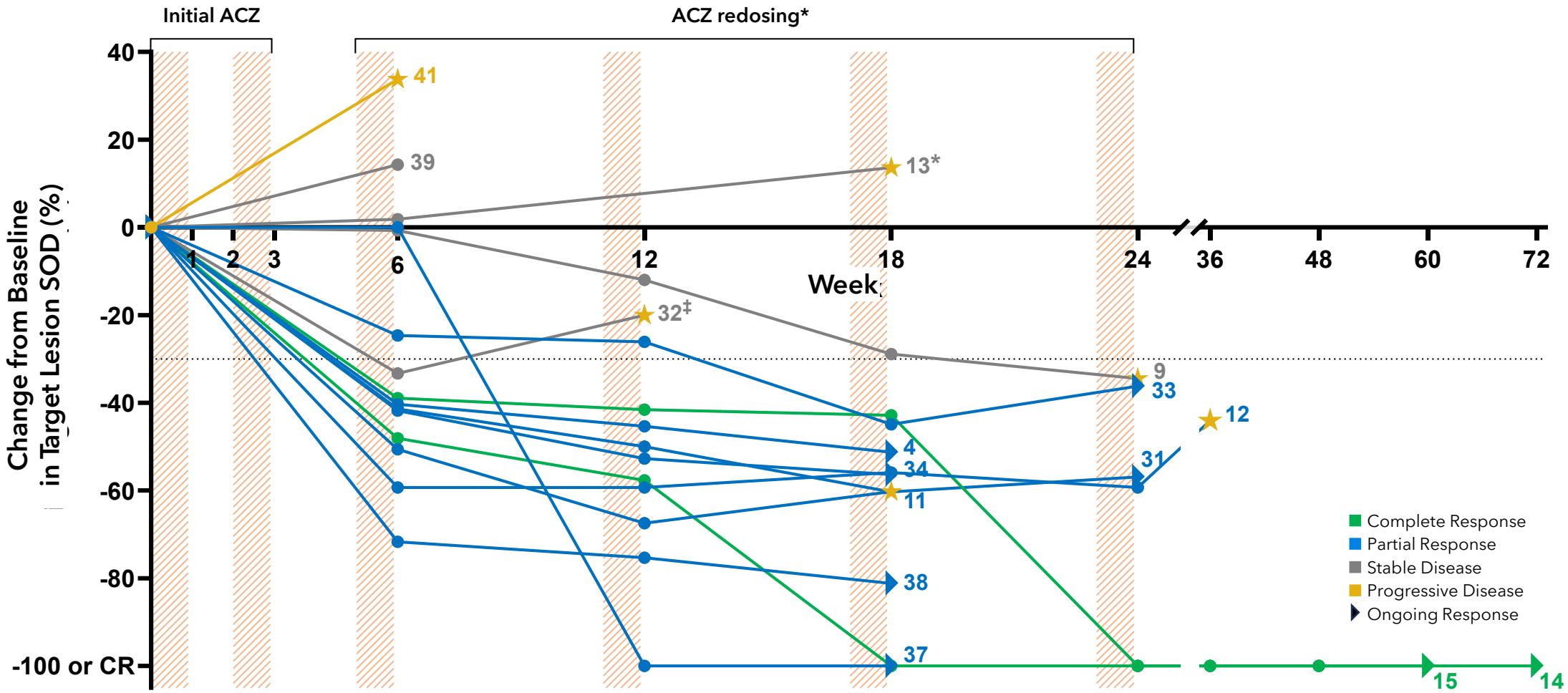
# Durable and Deepening Responses




Data cutoff: 22 January 2026. *Patient 13 did not receive ACZ redosing. ‡Patient 32 had BRAF-refractory small-volume disease and a new satellite lesion at Week 12 that was biopsy-proven.
ACZ, acetazolamide; CR, complete response; SOD, sum of diameters.



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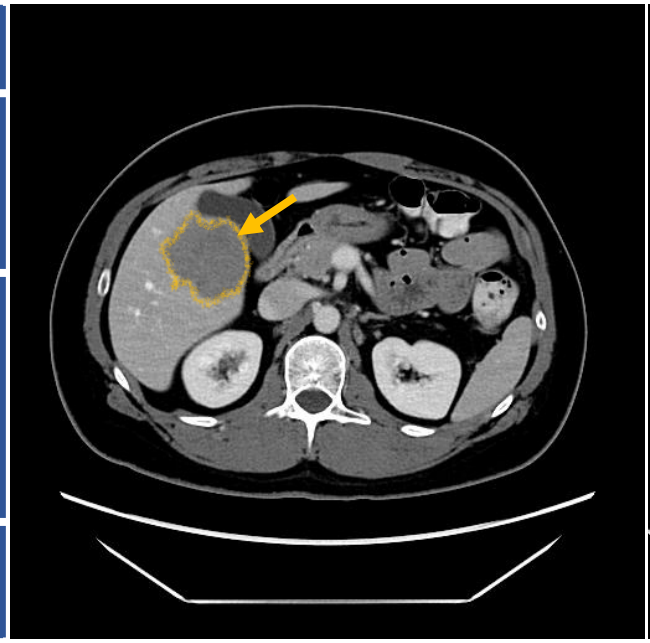
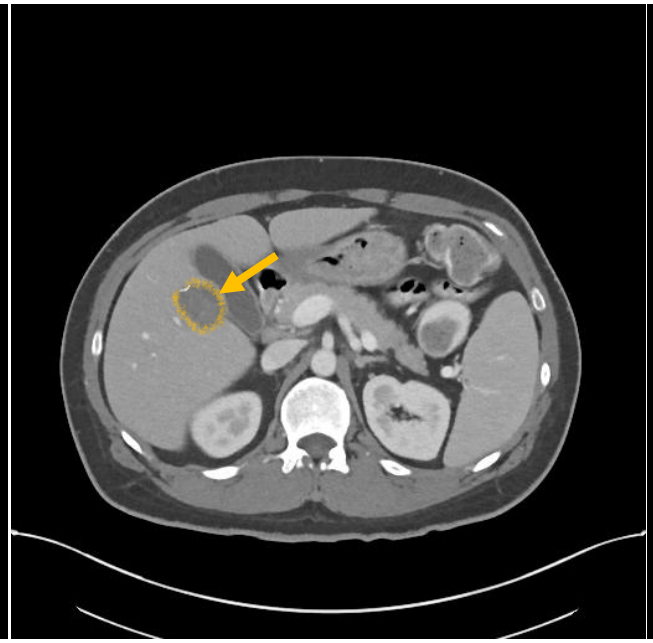
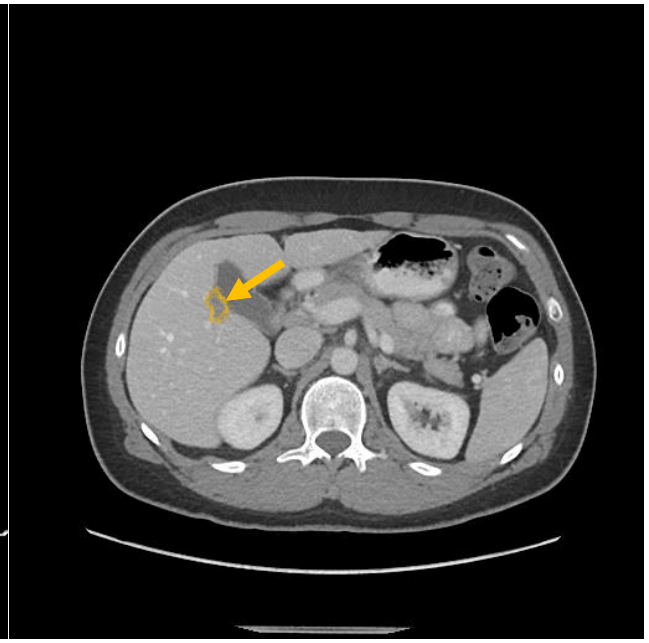
# Sustained and Deepening Reduction in Liver Lesion

**Patient 31: 44 yr-old with stage IV M1c rectal mucosal melanoma with liver metastases**

| | | | |
|---|---|---|---|
| LDH >ULN |  |  |  |
| Prior: **Ipi-Nivo (Primary resistant)** | | | |
| **Low-dose LD CNB TTP (liver)** 135 ×$10^9$ cells mfg 100 ×$10^9$ cells infused | | | |
| No Grade ≥3 TEAEs | | | |
| Target lesion: segment 5 liver metastasis | **Day -8** Baseline 58 × 53 mm | **Week 6: PR** **41%** target lesion SOD reduction | **Week 36: Ongoing PR** **60%** target lesion SOD reduction |

Data cutoff: 22 January 2026; Week 36 visit occurred on April 2, 2026 (after datacut).
CNB, core needle biopsy; LD, lymphodepletion; LDH, lactate dehydrogenase; PR, partial response; SOD, sum of diameters; TEAE, treatment-emergent adverse event; TTP, tumor tissue procurement; ULN, upper limit of normal.



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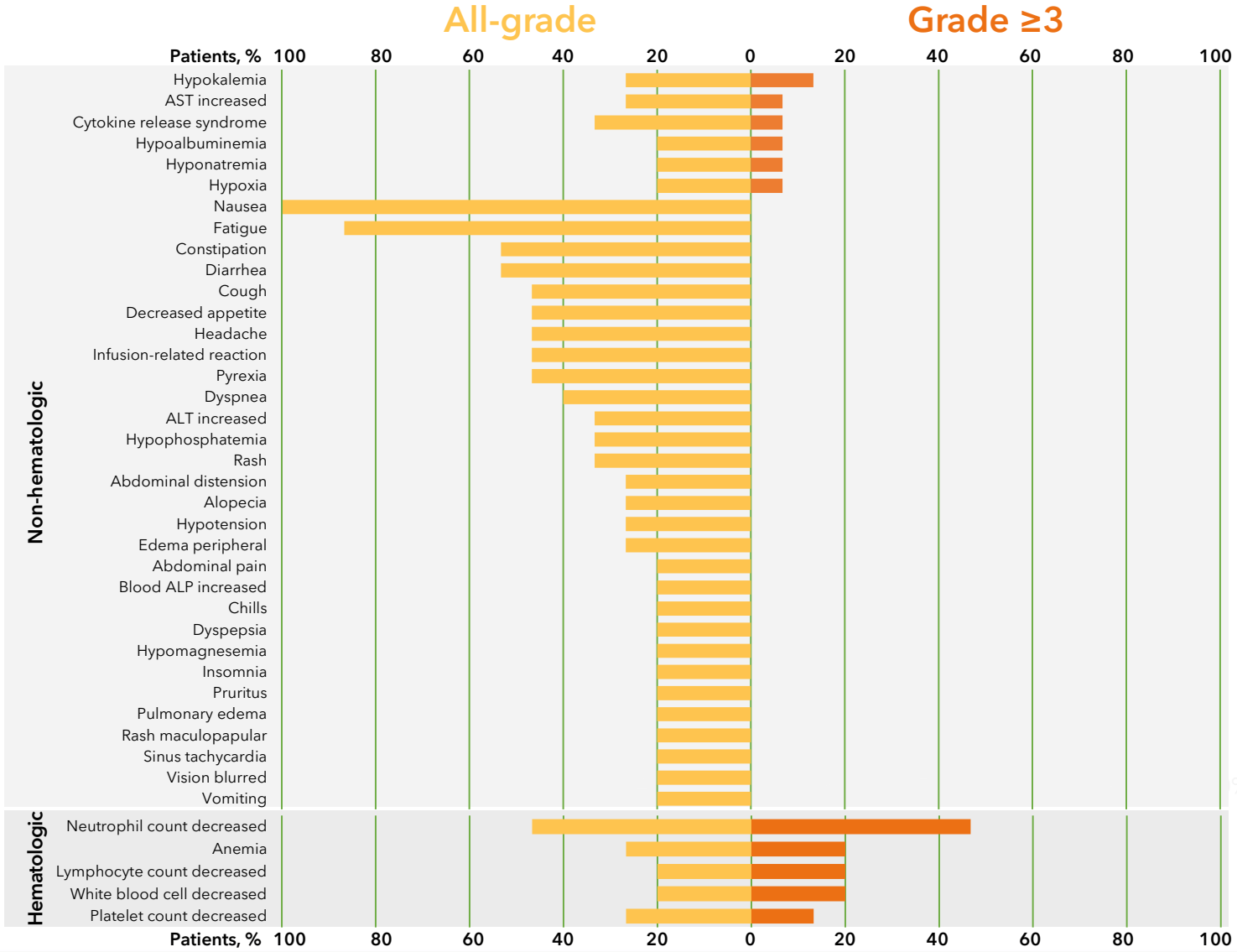
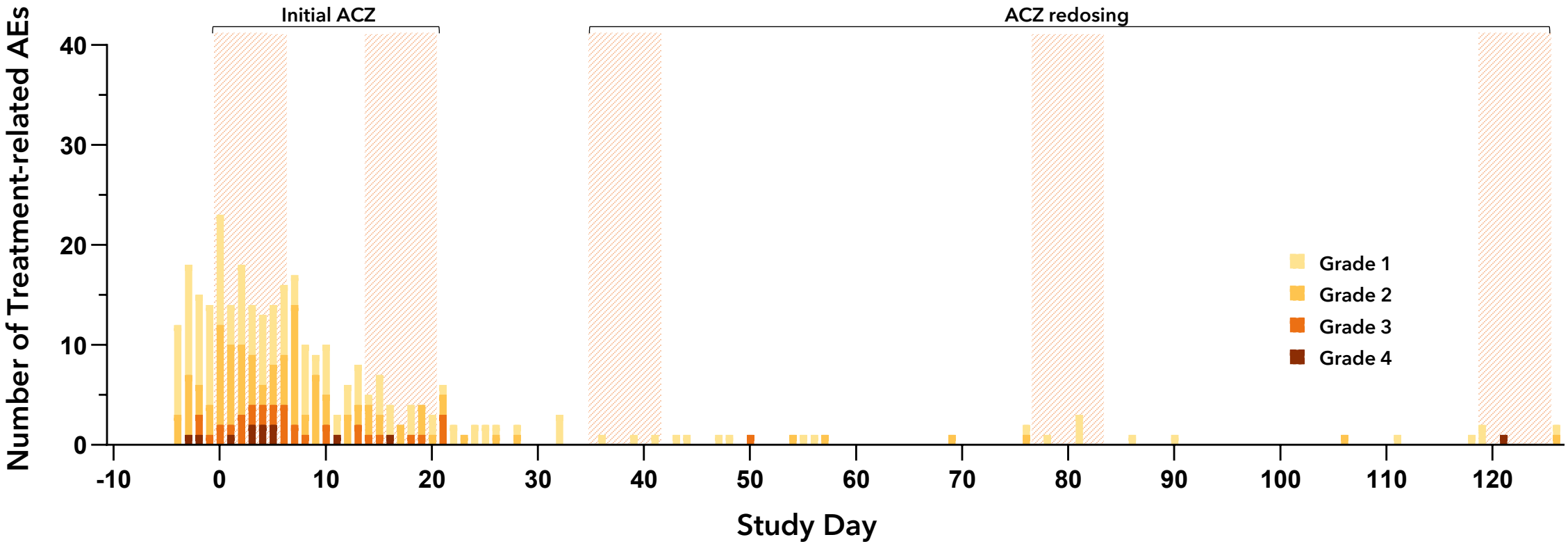
# TEAEs in ≥20% of Patients




- **Grade ≥3 non-hematologic toxicity was uncommon**
- **CRS** was reported for 5 patients (33%)
  - **1 event (7%) was Grade 3**
- **Hematologic toxicity was favorable**
  - 1 event (7%) of febrile neutropenia (Grade 3)
- **No DLTs**
- **No ICANS**
- **No ICU** transfer

Data cutoff: 22 January 2026. TEAE defined as any AE occurring after first dose of lymphodepletion, excluding AEs not related to OBX-115 or ACZ after Day 84. ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; ICANS, immune effector cell-associated neurotoxicity syndrome; ICU, intensive care unit; TEAE, treatment-emergent adverse event.

# TRAE Onset and Severity

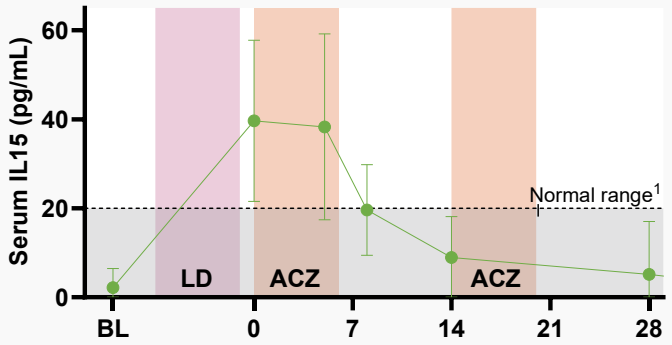



- TRAEs were **mostly Grade ≤2** and occurred in the first 2 weeks after infusion
- Longitudinal **ACZ redosing was well-tolerated** in outpatient setting
- **No treatment-related mortality**

Data cutoff: 22 January 2026. TRAE defined as any AE occurring after first dose of lymphodepletion assessed by investigator as possibly, probably, or definitely related to lymphodepletion, OBX-115, or ACZ.
ACZ, acetazolamide; AE, adverse event; TRAE, treatment-related adverse event.

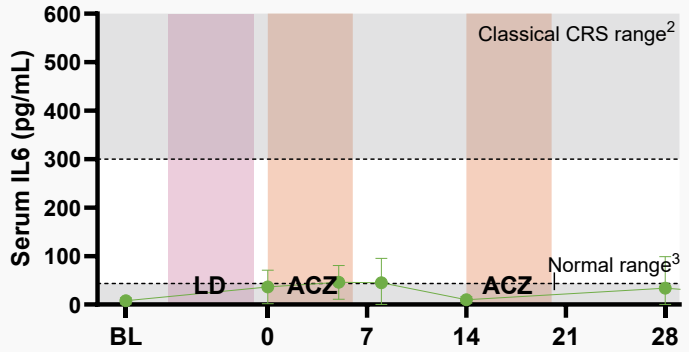
# Favorable Cytokine and ctDNA Profiles

## IL15



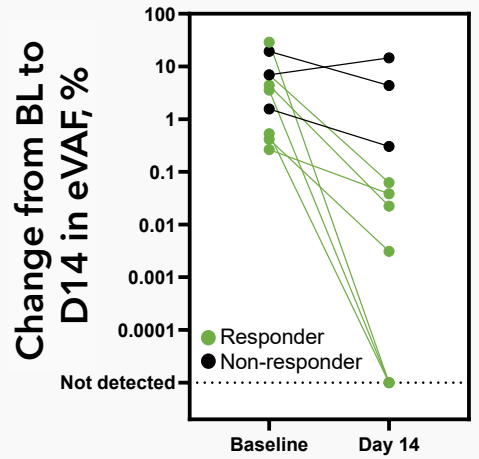

- Expected IL15 increase with lymphodepletion
- No IL15 elevation after OBX-115 infusion

## IL6




- IL6 remained well-below classical CRS range
- Tocilizumab not indicated for post-infusion CRS

## ctDNA




- ctDNA reduction by Day 14 in all responders, including 3 with ctDNA clearance

Data cutoff: 22 January 2026.

**1**. Lamana A et al. Eur Cytokine Netw. 2010 Sep;21(3):186-94. **2**. Pabst T et al. Exp Hematol. 2020;88:7–14. **3**. Said E et al. J Med Virol. 2021 Jun;93(6):3915-3924.

BL, Baseline; CRS, cytokine release syndrome; ctDNA, circulating tumor DNA; eVAF, estimated variant allele frequency; IL6, interleukin 6; IL15, interleukin 15; LD, lymphodepletion.

# Conclusions

- **OBX-115** engineered TIL cell therapy expressing regulatable mbIL15 potentially offers a **novel therapeutic intervention** for advanced melanoma that has progressed on/after ICI therapy, including ICI-combination–refractory disease
  - **ACZ-driven regulatable mbIL15** expression enables initial TIL expansion and potential long-term persistence through longitudinal redosing
- OBX-115 is characterized by a **differentiated safety profile** and **promising early efficacy**
  - Low rate of Grade 3+ non-hematologic AEs
  - **No DLTs, ICU** transfer, or **TRM**
  - **67% ORR**, including **2 complete responses**
  - **Median DOR not reached** (range, 1.1+, 14.9+ mo)
- OBX-115 may broaden the cell-therapy–eligible patient population
  - Option for **less-invasive core needle biopsy TTP**
  - Exclusively **low-dose lymphodepletion** compatible with **outpatient** administration
  - **Elimination of IL2** in the treatment regimen

ACZ, acetazolamide; AE, adverse event; DLT, dose-limiting toxicity; DOR, duration of response; ICI, immune checkpoint inhibitor; ICU, intensive care unit; IL2, interleukin 2; mbIL15, membrane-bound interleukin 15; ORR, objective response rate; TIL, tumor-infiltrating lymphocytes; TRM, treatment-related mortality; TTP, tumor tissue procurement.

# Key Takeaways

1

The OBX-115 **safety** profile is differentiated by exclusively **low-dose lymphodepletion** and **absence of IL2**

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Promising early **efficacy** was observed, with a **67% ORR** and potential for **durable** and **deepening** responses

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Key **regimen benefits** may provide a meaningful treatment option to a **broader patient population**

IL2, interleukin 2; ORR, objective response rate.

# Thank you

## Patients who participated in this trial, their caregivers, and their families

Study-site and sponsor personnel