OBSIDIAN
THERAPEUTICS

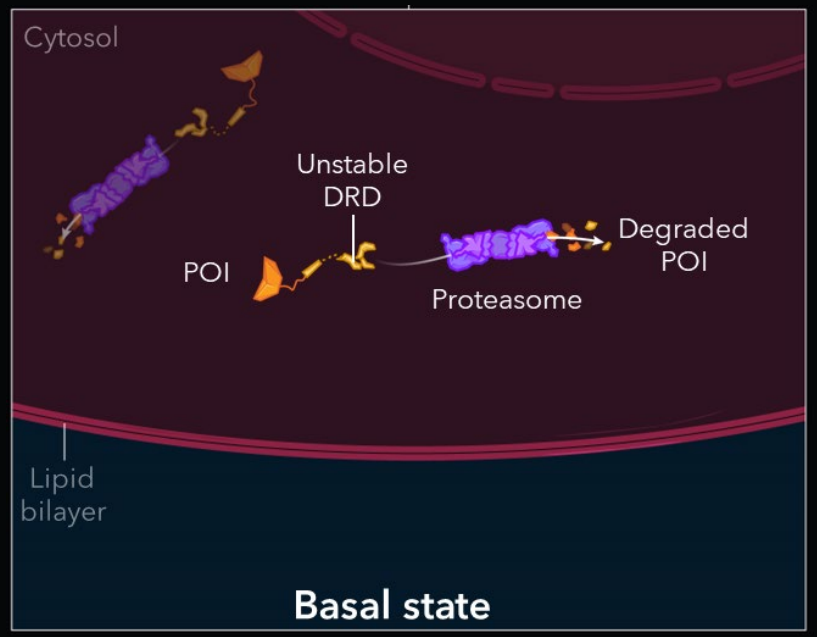
Obsidian Therapeutics Engineered TIL

cytoDRiVE Platform and OBX-115

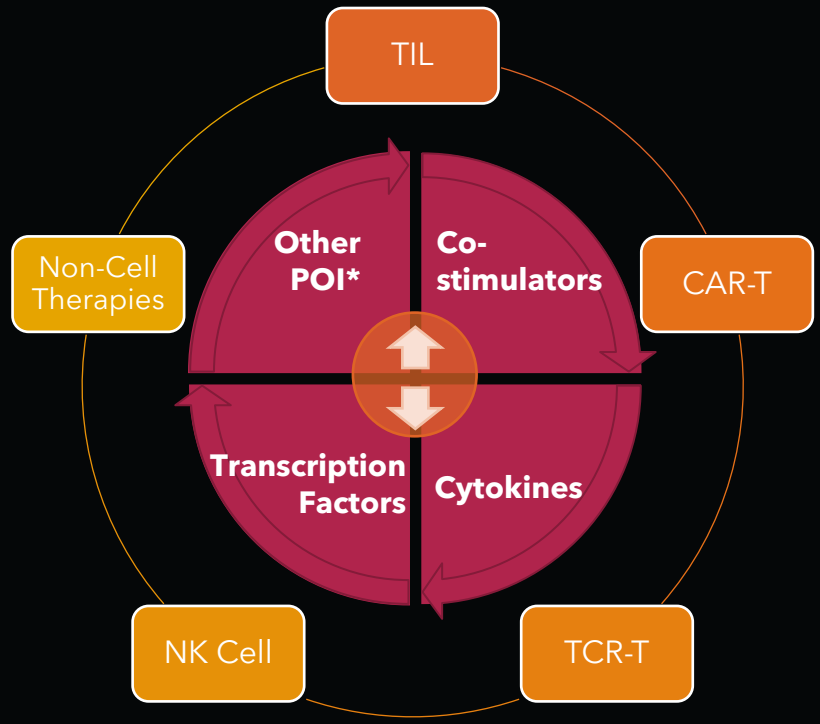
FEBRUARY 2025

cytoDRiVE Platform Unlocks Regulation of Armored Cell & Gene Therapy Products

cytoDRiVE Platform Regulates Any Protein of Interest



Unlocks the Universe of Regulatable Cell & Gene Therapy



Obsidian Experience: IL15, IL12, IL2, IL21, IFNα, IL18, 4-1BBL, CD40L, c-JUN, CAR and others, including co-regulation of 2 payloads in the same cell

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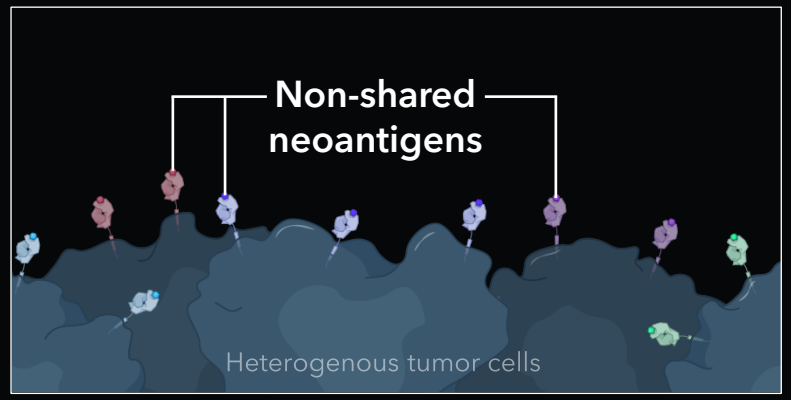
DRD, drug-responsive domain; POI, protein of interest; TIL, tumor-infiltrating lymphocytes.

Obsidian's Regulatable Armored TIL Cell Therapy[1] Addresses Limitations of Current Approaches in Solid Tumors



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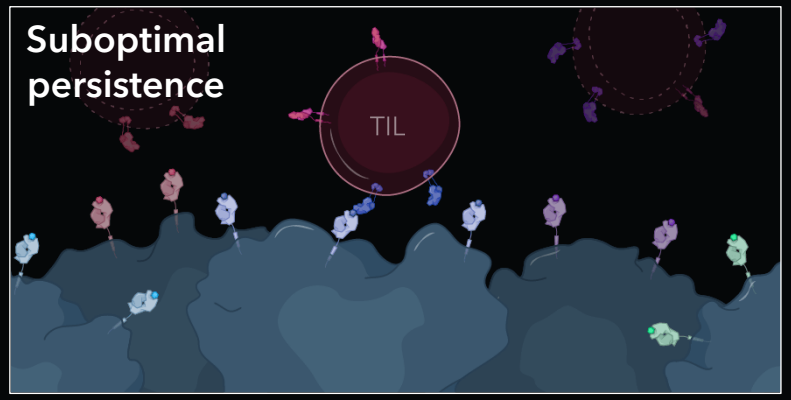
Critical challenge in treating solid tumors is overcoming numerous non-shared, tumor-specific neoantigens



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TIL traffic to tumor sites, naturally recognize multiple antigens and lyse patient's cancer cells…

…however, limited efficacy of non-engineered TIL cell therapies may be due to suboptimal expansion and persistence of infused TIL

Obsidian leverages cytoDRiVE® technology to regulate mbIL15
to improve antigen-independent expansion and persistence, which is expected to improve efficacy

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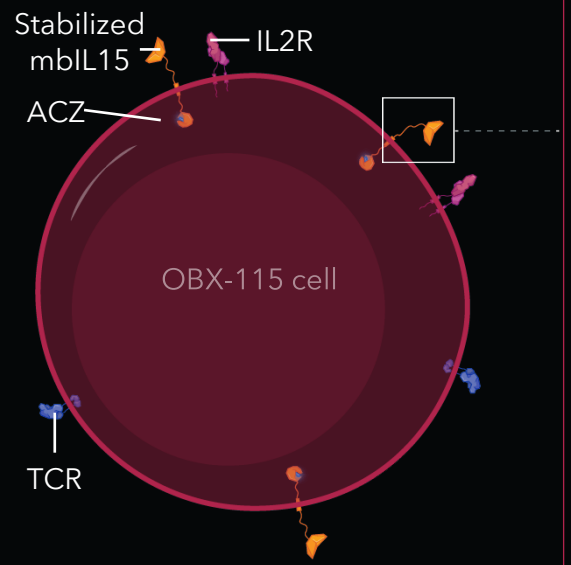
1. Obsidian's programs, including cytoTIL15™ TIL cell therapy product candidate (OBX-115), and cytoDRIVE® Platform are investigational and have not been approved by the FDA or any other regulatory agency.
mbIL15, membrane-bound interleukin 15; TIL, tumor-infiltrating lymphocytes.

mbIL15 Armoring Delivers a Superior Cell Therapy Product

OBX-115 is engineered with our proprietary mbIL15 gene construct with a flexible linker, which has unique signaling properties conferring the ability to drive both cis- and trans-cell activation



Benefits of IL15

Drives antigen-independent proliferation of memory CD8+ T-cells
Supports survival of CD8+ T cells without promoting terminal differentiation;
Drives antigen-independent proliferation of memory CD8+ T cells [1,2]

Sustains persistence and durable effector function
Provides efficient expansion of T cells without increasing cell exhaustion or compromising cytotoxicity [3]

Drives cytokine production and cytotoxicity
Sufficient to cause human memory CD8+ T cells to become highly cytolytic (increase perforin, granzyme B, IFNγ) [4]

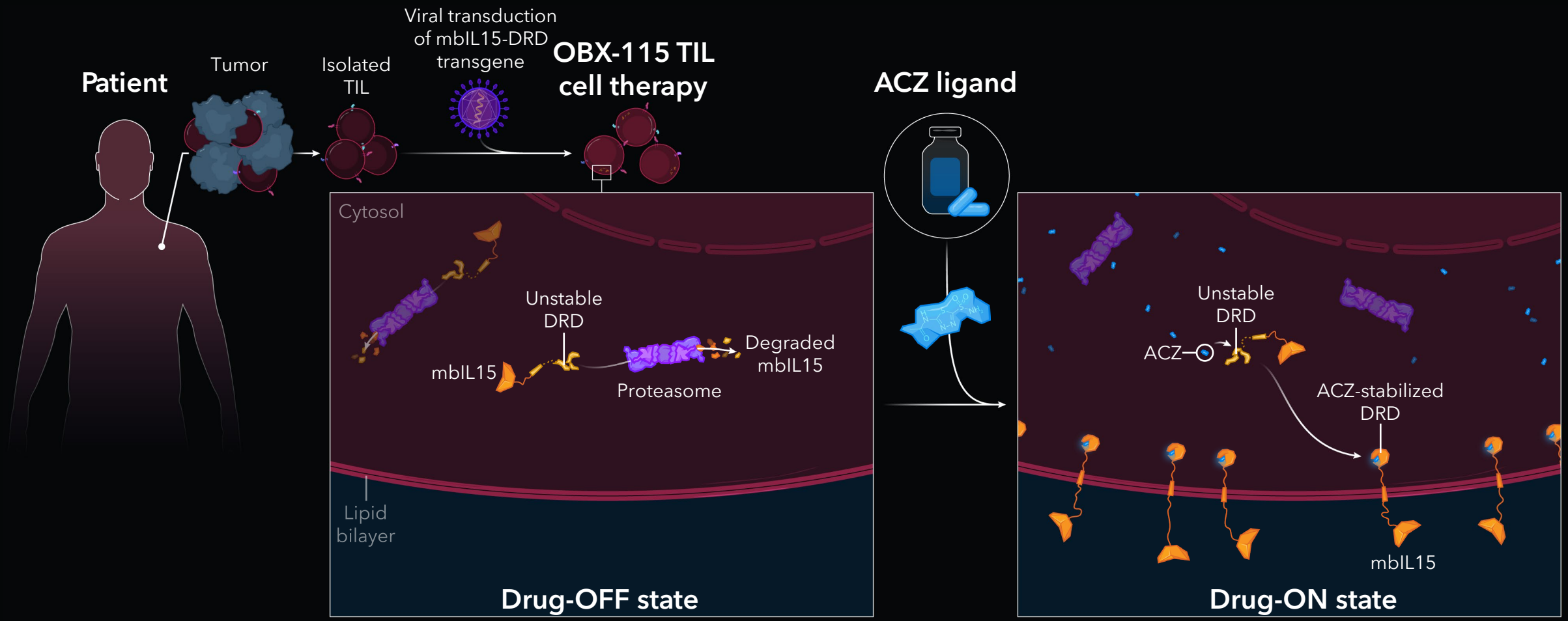
mbIL15 trans-activation drives engagement of other immune cells (e.g., NK cells), potentially preventing tumor escape from MHC loss
Supports NK cell homeostasis and proliferation and supports the survival of activated NK cells [5];
Shown to increase cell expansion and persistence of NK cell therapies [6]

Does not support Treg development in the TME [7]
Lack of Tregs decreases the risk of an immune-suppressive TME

Potential for reduced-dose lymphodepletion
Reduced dependence on homeostatic IL15 increase after lymphodepletion to drive expansion [8]

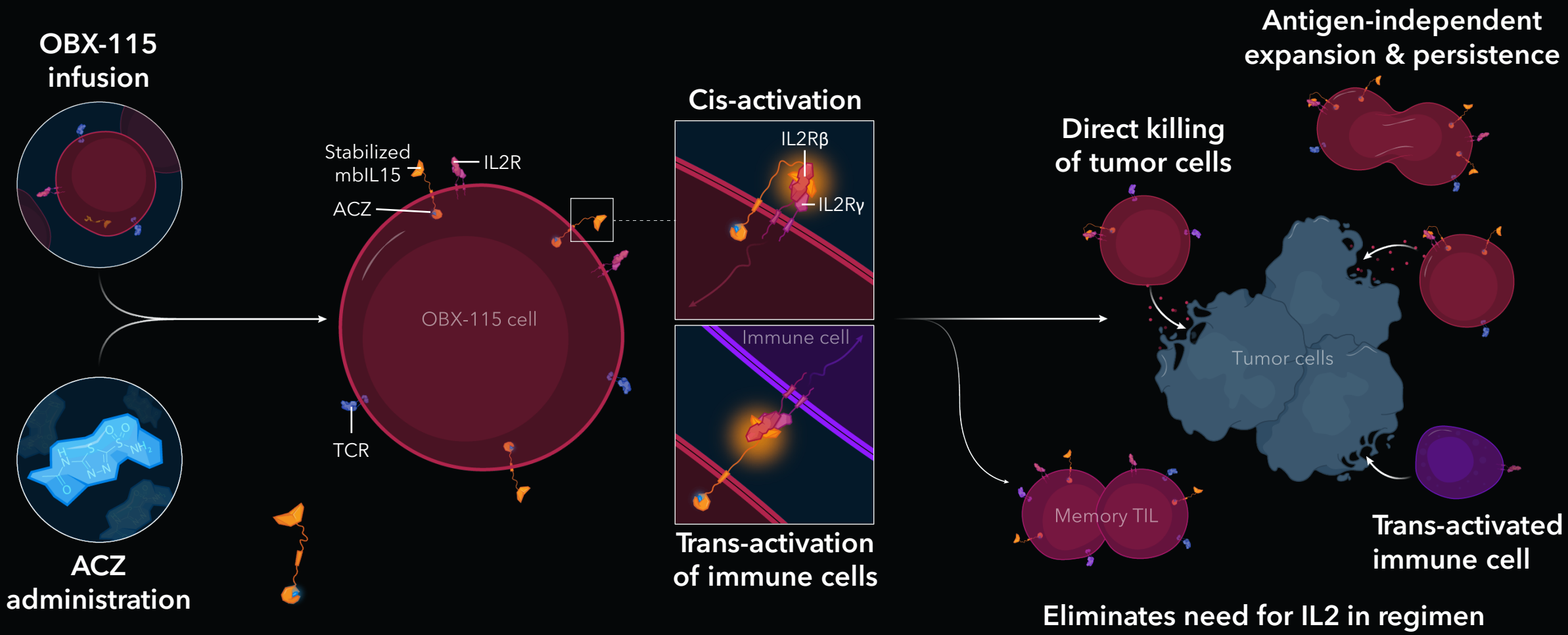
1. Schluns, K et al., J. Immunol. 168: 4827-4831 (2002). 2. Berard, M. et al., J Immunol 2003; 170:5018-5026 (2003). 3. Blood. 2006 Jul 15;108(2):600-8). 4. Cheuk, S. et al., Immunity 46, 287–300 (2017). 5. Ma, S 2022 Trends in Immunology, 43:10, p. 833-8475. 6. Leukemia 32, 520–531 (2018)). 7. Ma A, Annu Rev Immunol. 2006;24:657-79. 8. Dudley et al. J Clin Oncol 2008 Nov 10;26(32):5233.

Leveraging Our cytoDRiVE® Platform to Regulate mbIL15 Activity Using the FDA-approved Small-molecule Drug ACZ



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

OBX-115: Addressing Limitations of Non-engineered TIL



ACZ, acetazolamide; mb, membrane-bound; MOA, mechanism of action; TCR, T-cell receptor; TIL, tumor-infiltrating lymphocytes.

Proprietary Manufacturing: mbIL15 Drives a CD8+ Enriched and Minimally Exhausted Product With Enhanced Memory Phenotype

CD8+ enriched, minimally exhausted OBX-115[1] product

Tumor tissue procurement
Core needle biopsy supported

Optimized pre-REP

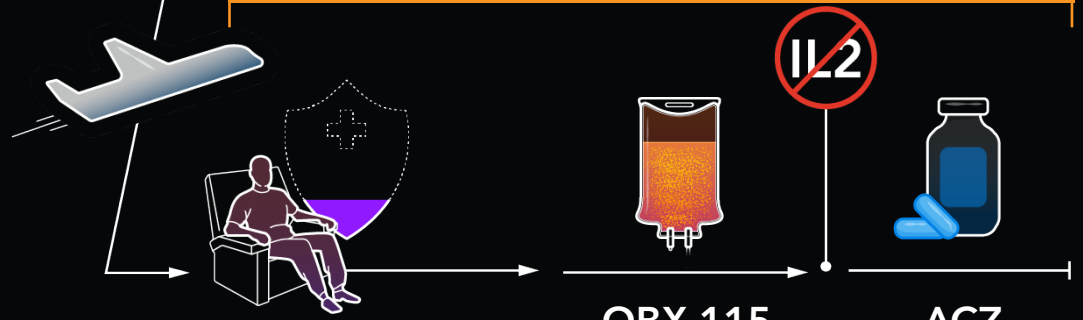
Activation/ transduction
Anti-CD3 Ab
Retroviral vector

Proprietary, optimized REP
iFeeder cells expressing IL21 and 4-1BBL
ACZ (no IL2)

Cryo-preservation

Reproducible and consistent drug product
Positioned to be scalable for commercialization

OBX-115 cell therapy regimen



Lymphodepletion*

OBX-115 infusion

ACZ dosing

Obsidian's programs, including OBX-115, and cytoDRIVE® Platform are investigational and have not been approved by the FDA or any other regulatory agency.*Standard-dose lymphodepletion (5-day regimen: Cy, 60 mg/kg × 2 days; Flu, 25 mg/m² × 5 days) or low-dose lymphodepletion (4-day regimen: Cy, 750 mg/m² × 3 days; Flu, 30 mg/m² × 4 days).
Ab, antibody; ACZ, acetazolamide; CMC, chemistry, manufacturing, and controls; IL2, interleukin 2; REP, rapid expansion protocol; TIL, tumor-infiltrating lymphocytes.

