

# Trial in Progress: A Phase 1/2 Study to Investigate the Safety and Efficacy of OBX-115 Engineered Tumor-infiltrating Lymphocyte (TIL) Cell Therapy in Patients with Advanced Solid Tumors (Agni-01)

Adam J Schoenfeld,<sup>1</sup> Allison Betof Warner,<sup>2</sup> Jason A Chesney,<sup>3</sup> Sajeve S Thomas,<sup>4</sup> Omid Hamid,<sup>5</sup> Gino K In,<sup>6</sup> Alexander N Shoushtari,<sup>1</sup> Yazan Samhouri,<sup>7</sup> Parameswaran Hari,<sup>8</sup> Giridharan Ramsingh,<sup>8</sup> Prakash Prabhakar,<sup>8</sup> Lauren McLaughlin,<sup>8</sup> Kai He<sup>9</sup>

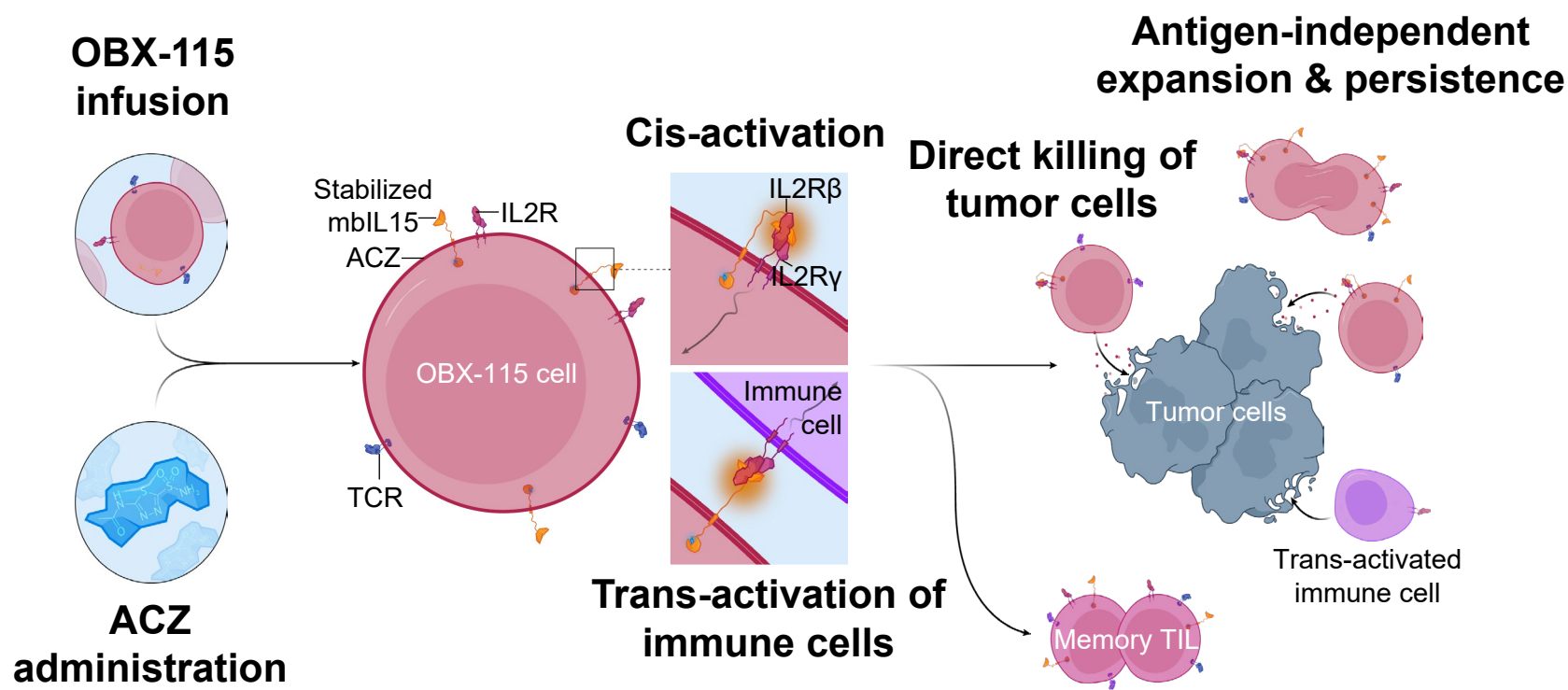
1. Memorial Sloan Kettering Cancer Center, New York, NY; 2. Stanford University School of Medicine, Stanford, CA, USA; 3. UofL Health – Brown Cancer Center, Louisville, KY, USA; 4. Orlando Health Cancer Institute, Orlando, FL, USA; 5. The Angeles Clinic and Research Institute, Cedars-Sinai, Los Angeles, CA, USA; 6. Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA; 7. Allegheny Health Network Cancer Institute, Pittsburgh, PA, USA; 8. Obsidian Therapeutics, Cambridge, MA, USA; 9. The Ohio State University Comprehensive Cancer Center, The Ohio State University College of Medicine, Columbus, OH, USA

PHari@obsidiantx.com

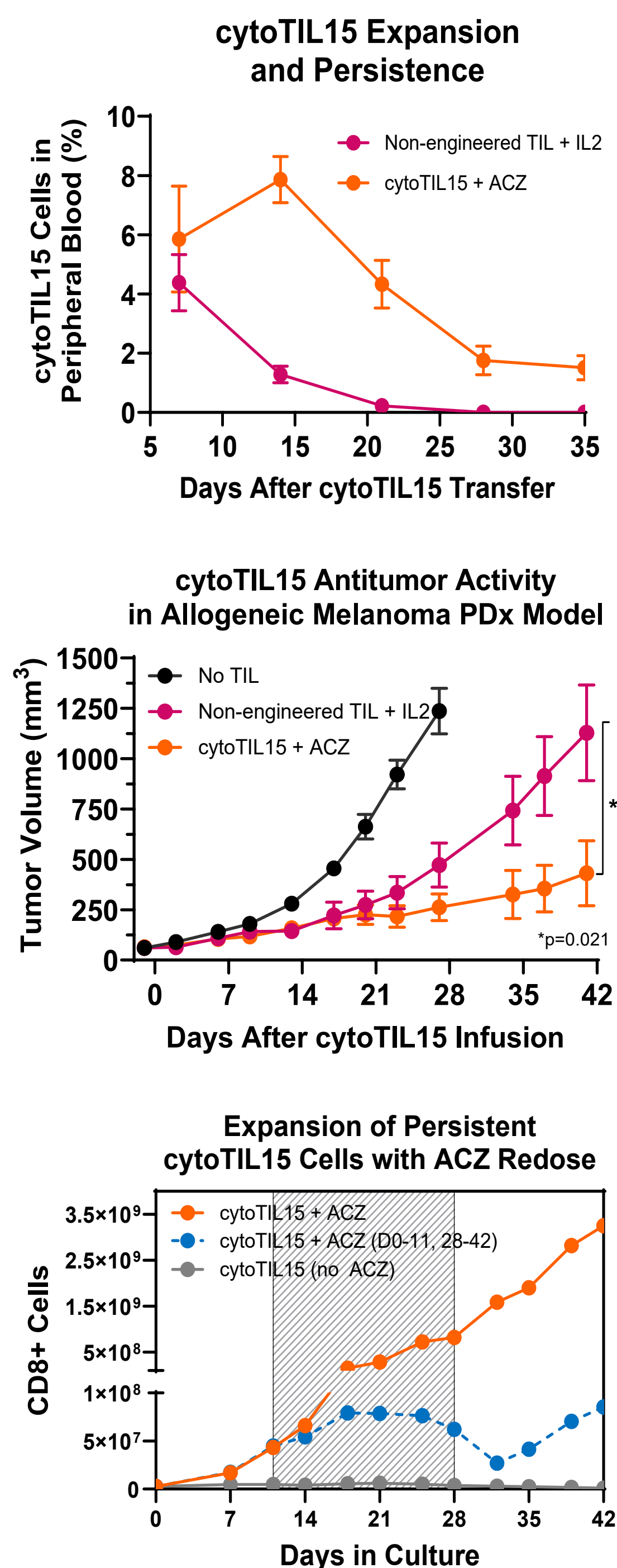
## Introduction

- Immune checkpoint inhibitors (ICI) have improved treatment outcomes for patients with melanoma and non-small cell lung cancer (NSCLC); however, most patients do not achieve long-term survival
- Lifileucel, a non-engineered tumor-derived autologous T-cell immunotherapy (tumor-infiltrating lymphocyte [TIL] cell therapy), was recently FDA-approved for anti-PD-1-experienced unresectable or metastatic melanoma<sup>1</sup> and has shown promising activity in this setting (ORR, 31.5%; mDOR NR), but is associated with a treatment-related mortality rate of 7.5%<sup>2</sup>
- Lifileucel is also being investigated in patients with ICI-resistant advanced NSCLC, and a response rate of 21% has been reported<sup>3</sup>
- All non-engineered TIL cell therapies require high-dose interleukin 2 (IL2), which has well-described high-grade toxicity<sup>2,4,5</sup> limiting patient eligibility and frequently requiring specialized management
- OBX-115 TIL are engineered to express mbIL15 fused to a drug-responsive domain, which allows for a dose-dependent increase in functional mbIL15 levels in the presence of an FDA-approved stabilizing drug (acetazolamide [ACZ]), avoiding the need for IL2 (Figure 1)
- In preclinical studies, cytoTIL15<sup>TM</sup> TIL (OBX-115) in the presence of ACZ demonstrated enhanced proliferation, persistence, and antitumor activity compared with non-engineered TIL + IL2<sup>6,7</sup> (Figure 2)
- The current study (Agni-01 [NCT06060613]) is enrolling at multiple US sites using centralized manufacturing

### Figure 1. OBX-115 Mechanism of Action



### Figure 2. Preclinical Data

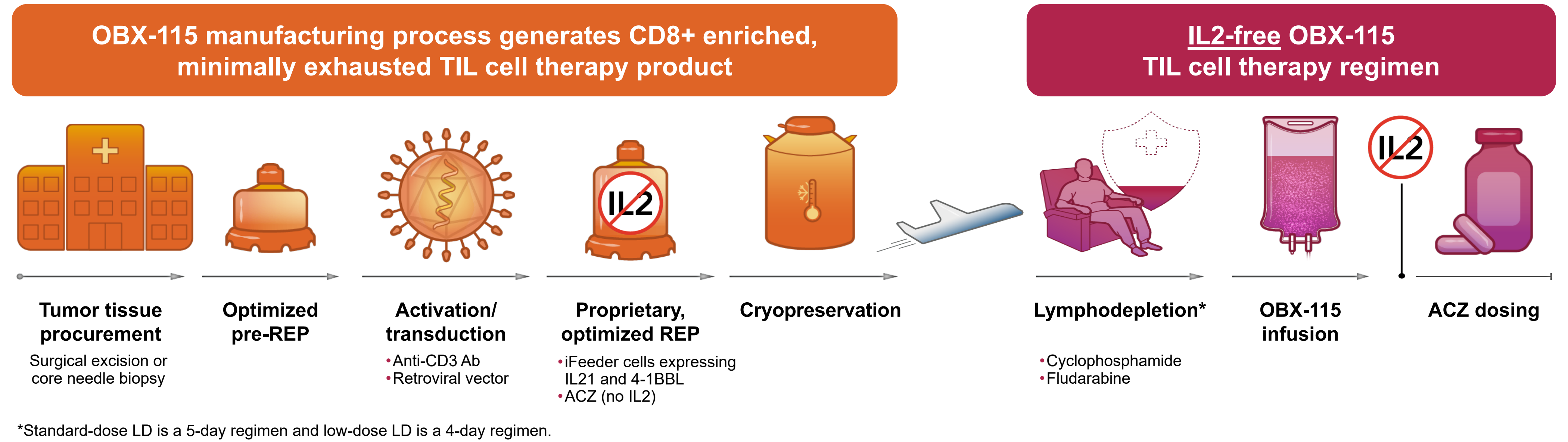


## Study Design

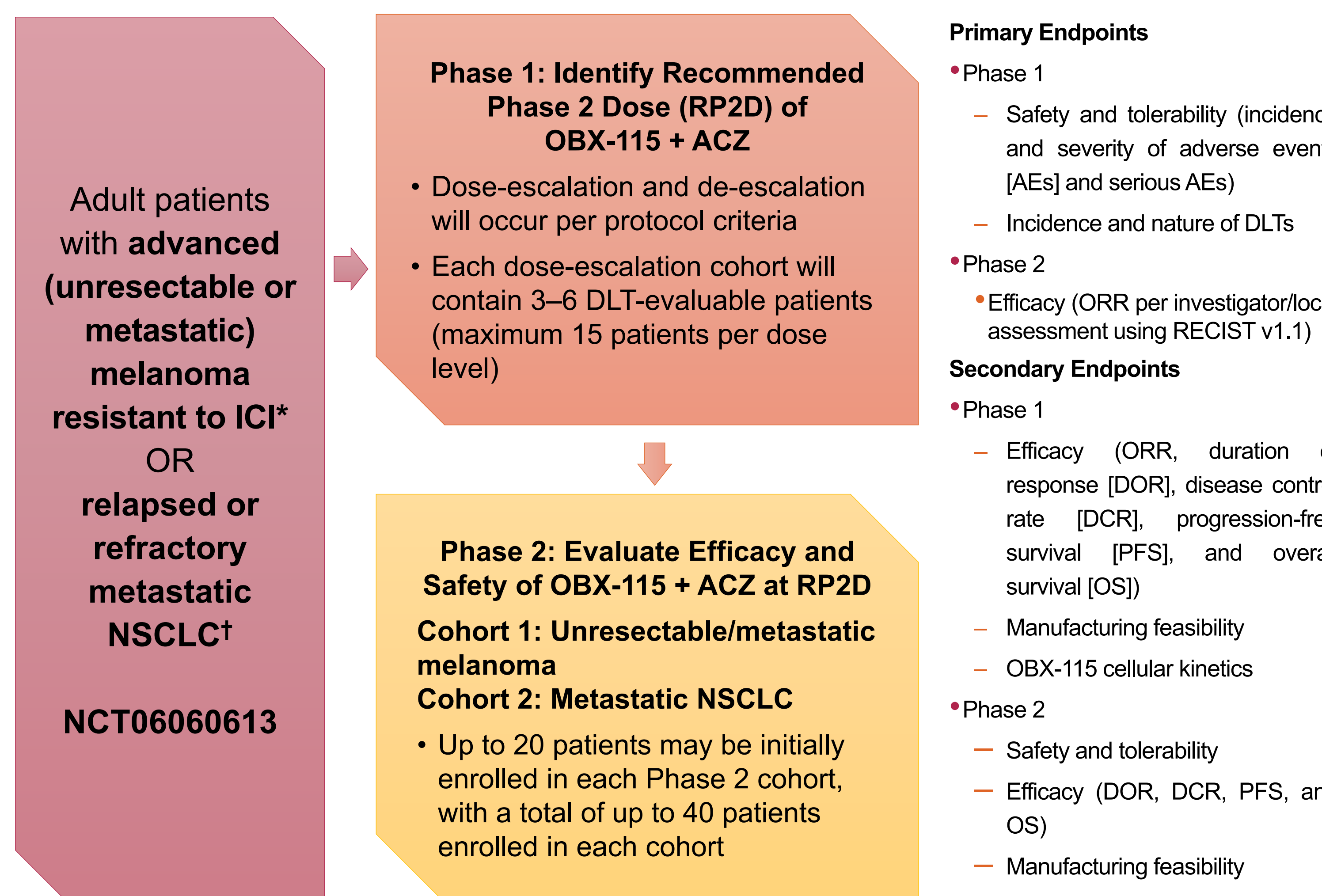
This single-arm, open-label, nonrandomized, multicenter study will assess the safety, tolerability, and efficacy of the autologous OBX-115 engineered TIL cell therapy regimen in patients with advanced solid tumors

- Cryopreserved OBX-115 is manufactured using the patient's own tumor tissue, procured by either surgical excision or core needle biopsy, and is infused intravenously following standard- or low-dose (based on clinical eligibility) lymphodepletion with cyclophosphamide and fludarabine (Figure 3)
- ACZ is administered orally at cohort-defined doses once daily for up to 14 days. Additional ACZ is dosed for up to 14 days at Week 6 (all patients), with optional redosing at Weeks 12 and 18 if an optimal response is not achieved (NSCLC only), and upon progression (all patients) when new anticancer therapy is not immediately warranted (Figures 4–5)
- No IL2 is administered

### Figure 3. Centralized OBX-115 Manufacturing and Patient Journey

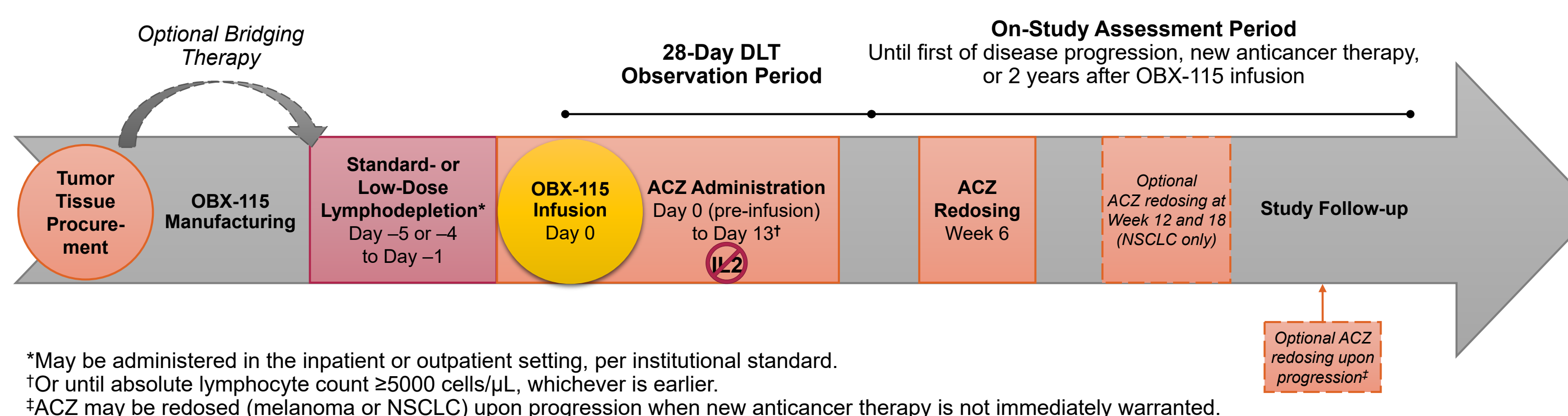


### Figure 4. Study Overview



\*Patients with BRAF-mutated disease must have received BRAF inhibitor ± MEK inhibitor therapy.  
†Prior treatment should include an approved ICI-based regimen and/or an approved targeted therapy in appropriate patients.

### Figure 5. Study Treatment Schema



\*May be administered in the inpatient or outpatient setting, per institutional standard.  
†Or until absolute lymphocyte count ≥5000 cells/μL, whichever is earlier.  
‡ACZ may be redosed (melanoma or NSCLC) upon progression when new anticancer therapy is not immediately warranted.

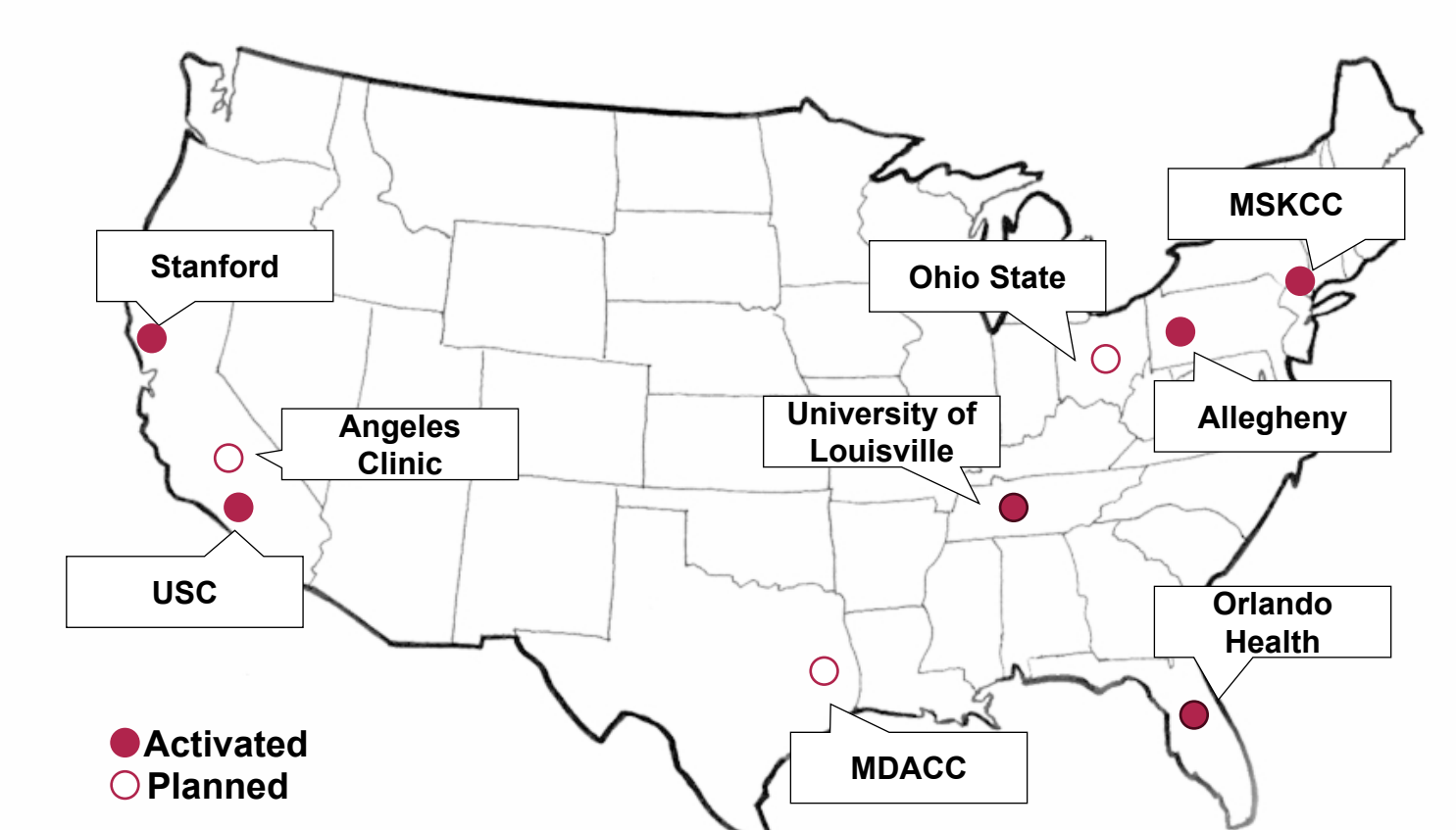
### Key Inclusion Criteria

- Age ≥18 years
- Histologically confirmed diagnosis of melanoma or NSCLC:
  - Unresectable Stage IIIC, IIID, or Stage IV metastatic melanoma with documented radiographic disease progression after systemic therapy containing a PD-1- or PD-L1-blocking antibody (if adjuvant setting, progression during or within 12 weeks after the last dose) and received a BRAF inhibitor ± MEK inhibitor if BRAF V600 mutation-positive
  - Metastatic NSCLC previously treated with an approved systemic therapy for metastatic disease (including an ICI-based regimen and/or targeted therapy where applicable) and progressed or is no longer deriving benefit, or is unable to continue due to treatment intolerance
- ≥1 lesion suitable for OBX-115 manufacturing with expected minimum of 1.5-cm diameter
- Minimally invasive tumor tissue procurement (core needle biopsy) may be considered on a case-by-case basis
- ≥1 RECIST v1.1-measurable lesion remaining after tumor tissue procurement
- ECOG performance status 0 or 1
- Estimated life expectancy >6 months

### Key Exclusion Criteria

- Uveal melanoma
- Active autoimmune disease, including active uveitis or any other medical illness that would pose increased risks for study participation
- History of brain metastases or leptomeningeal disease; patients with brain metastases that are ≤1.5-cm diameter that have been treated and are asymptomatic may be eligible
- Prior allogeneic organ transplant, allogeneic cell therapy, or genetically engineered cell therapy (not including autologous stem cell or non-engineered TIL cell therapy)
- Systemic steroid therapy >10 mg/day of prednisone or equivalent

### Figure 6. Study Locations



## References

- US Food and Drug Administration Center for Biologics Evaluation and Research (CBER). AMTAGVI Accelerated BLA Approval (https://www.fda.gov/media/176418/download).
- US Food and Drug Administration Center for Biologics Evaluation and Research (CBER). AMTAGVI Prescribing Information (https://www.fda.gov/media/176417/download).
- Schoenfeld AJ, et al. Cancer Discov 2024 Apr 2. Epub ahead of print.
- Rohaan MW, et al. N Engl J Med 2022;387(23):2113-2125.
- Chesney J, et al. J Immunother Cancer 2022;10(12). DOI: 10.1136/jitc-2022-005755.
- Burga R, et al. Emerging Cellular Therapies at the Forefront of Cancer Immunotherapy. Fairmont Banff Springs, Alberta, Canada: Keystone Symposia; 2023.
- Pedro K, et al. AACR Annual Meeting 2023. Orlando, FL: Cancer Research; 2023:LB096.

## Abbreviations

Ab, antibody; ACZ, acetazolamide; AE, adverse event; DCR, disease control rate; DOR, duration of response; DLT, dose-limiting toxicity; ECG, electrocardiogram; ECOG, Eastern Cooperative Oncology Group; ICI, immune checkpoint inhibitors; IL2, interleukin 2; IL2R, interleukin 2 receptor; mbIL15, membrane-bound interleukin 15; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein-1; PD-L1, programmed death ligand 1; PFS, progression-free survival; PR, partial response; QD, daily; RECIST, Response Evaluation Criteria in Solid Tumors; REP, rapid expansion protocol; RP2D, recommended phase 2 dose; TCR, T-cell receptor; TIL, tumor-infiltrating lymphocytes.

## Disclosures

Adam J Schoenfeld reports consulting or advisory roles with Johnson & Johnson/Janssen, KSQ Therapeutics, Perceptive Advisors, Heat Biologics, Bristol-Myers Squibb, Enara Bio, Umoja Biopharma, Oppenheimer, Iovance Biotherapeutics, Lyell Immunopharma, Merck, Immunocore, Legend Biotech, Amgen, and Prelude Therapeutics; travel, accommodations, or expenses from Iovance Biotherapeutics and Instil Bio; research funding from GlaxoSmithKline, Merck, Bristol-Myers Squibb, Iovance Biotherapeutics, Achilles Therapeutics, Amgen, PACT Pharma, Harpoon Therapeutics, and Instil Bio; and other relationship with Merck, Bristol-Myers Squibb, Iovance Biotherapeutics, PACT Pharma, Achilles Therapeutics, GlaxoSmithKline, Harpoon Therapeutics, Amgen, and Instil Bio.

## Acknowledgments

The authors thank the patients, their families, and investigators who participate in the study. This study is funded by Obsidian Therapeutics, Inc. (Cambridge, MA, USA). Editorial assistance was provided by Amanda Kelly and funded by Obsidian Therapeutics, Inc. (Cambridge, MA, USA).

