Obsidian Therapeutics Announces Positive Clinical Data from OBX-115 in Patients with Advanced Melanoma in Ongoing Multicenter Study at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting

June 2, 2025

- *Oral presentation of Phase 1 results from Agni-01 multicenter study of cryopreserved OBX-115, a novel IL2-sparing engineered TIL cell therapy armored with pharmacologically regulatable membrane-bound IL15 (mbIL15), in patients with ICI-resistant advanced melanoma (n=11)*
- *OBX-115 ORR was 67% at recommended Phase 2 dose (RP2D) (n=6), including 1 CR*
- *OBX-115 safety profile remains consistent: no DLTs, no treatment-related ICU transfer, no treatment-related mortality*
- *10 of 11 of patients were treated with low-dose lymphodepletion, including 1 in outpatient setting*

CAMBRIDGE, Mass., June 2, 2025 – Obsidian Therapeutics, Inc., a clinical-stage biotechnology company pioneering engineered cell and gene therapies, today announced initial Phase 1 safety and efficacy data from the Phase 1/2 Agni-01 multicenter study of OBX-115, a novel engineered tumor-derived autologous T cell immunotherapy (tumor-infiltrating lymphocyte [TIL] cell therapy) armored with pharmacologically regulatable membrane-bound IL15 (mbIL15), in patients with immune checkpoint inhibitor (ICI)-resistant advanced or metastatic melanoma (NCT06060613). These data, summarized below, will be presented in a rapid oral presentation (abstract 9517) delivered by Jason A. Chesney, M.D., Ph.D., Director and Chief Administrative Officer of UofL Health – Brown Cancer Center/Oncology Service Line at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting.

Obsidian is also presenting a poster for abstract 9519 summarizing translational data from the Phase 1 first-in-human single-center study of OBX-115 (NCT05470283, enrollment completed) in ICI-resistant advanced melanoma.

Summary of OBX-115 Safety and Efficacy Data (March 26, 2025 data cutoff):

Advancing a More Patient-centric TIL Cell Therapy Regimen in Heavily Pre-treated Advanced Melanoma Patient Population

- Patients had disease that was predominantly ICI primary-resistant, with a median of 4 (range, 1–6) lines of prior systemic therapy, including a median of 2 (1–5) lines of prior ICI therapy (n=11).
- 10 patients received low-dose lymphodepletion (approximately 50% less Cyclophosphamide relative to non-engineered TIL), including 1 in the outpatient setting.
- Acetazolamide (ACZ) redosing following initial OBX-115 infusion to drive re-activation of OBX-115 cells was tolerable and safe enough to administer at home.

OBX-115 Continues to Deliver Positively Differentiated Safety Profile Relative to Non-engineered TIL; No IL2, No Treatment-related Mortality:

- No dose-limiting toxicities were observed at any dose level.
- No Grade 4 or higher nonhematologic treatment-related adverse events (TRAEs) were reported; 5 patients experienced limited Grade 3 nonhematologic TRAEs.
- No confirmed events of cytokine release syndrome or infusion-related reaction higher than Grade 2; no capillary leak syndrome or immune effector cell-associated neurotoxicity syndrome were reported.
- No treatment-related ICU transfer, no treatment-related mortality.

OBX-115 Maintains Consistent Efficacy Profile Without IL2 and With Low-dose Lymphodepletion in Anti-PD-1-resistant Advanced Melanoma; Dose Level 3 (RP2D) To Be Further Explored in Phase 2

- Encouraging efficacy profile observed at the RP2D (n=6)
  - 66.7% ORR, including 1 confirmed CR and 3 confirmed PRs (investigator-assessed RECIST 1.1 criteria)
  - Durable clinical benefit, including 3 of 4 responses ongoing at week 24 / data cutoff (median duration of response not reached)
  - 100% disease control rate, defined as stable disease or better for ≥12 weeks post-infusion
- 36.4% objective response rate (ORR) across all dose levels (n=11)
- Majority had reduction in tumor burden reduction: 83% at RP2D; 73% across all dose levels.

Dr. Chesney commented, “It is very encouraging to see the promising safety and efficacy profile for OBX-115, now observed in the Agni-01 multicenter study. As a highly differentiated, IL2-sparing TIL cell therapy that is compatible with low-dose lymphodepletion,

OBX-115 has the potential to transform the treatment landscape and broaden the eligible population for patients with high unmet need."

"The exciting results from OBX-115 in ICI-resistant advanced melanoma further indicate that OBX-115 has promising therapeutic potential, and that ACZ redosing is well-tolerated and has the potential to re-activate and re-expand persistent OBX-115 TIL," commented Parameswaran Hari, M.D., Chief Development Officer of Obsidian. "We look forward to exploring the go-forward melanoma RP2D in Phase 2, and continuing to evaluate OBX-115 in a Phase 1 cohort of patients with advanced non-small cell lung cancer, where we believe the potential impact from an IL2-sparing TIL cell therapy is clinically significant and may expand patient eligibility."

Obsidian is actively enrolling patients with advanced or metastatic melanoma and non-small cell lung cancer (NSCLC) at multiple sites in its ongoing Phase 1/2 Agni-01 multicenter study. Additional details may be found at clinicaltrials.gov, using identifier: NCT06060613.

About OBX-115

Obsidian's lead investigational cytoTIL15™ program, OBX-115, is a novel engineered tumor-derived autologous T cell immunotherapy (tumor-infiltrating lymphocyte [TIL] cell therapy) armored with pharmacologically regulatable membrane-bound IL15 (mbIL15). OBX-115 has the potential to become a meaningful therapeutic option for patients with advanced or metastatic melanoma and other solid tumors by leveraging the expected benefits of mbIL15 and Obsidian's proprietary, differentiated manufacturing process to enhance persistence, antitumor activity, and clinical safety of TIL cell therapy. Obsidian is investigating OBX-115 in the phase 1/2 Agni-01 multicenter trial in patients with advanced solid tumors (NCT06060613).

About Obsidian Therapeutics

Obsidian Therapeutics, Inc. is a clinical-stage biotechnology company pioneering engineered cell and gene therapies to deliver transformative outcomes for patients with intractable diseases. Obsidian's proprietary cytoDRiVE® technology is designed to precisely regulate the timing and level of protein function by using FDA-approved small-molecule drugs. Obsidian is headquartered in Cambridge, MA. For more information, please visit www.obsidiantx.com and follow us on LinkedIn.

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