Sensei Biotherapeutics Reports Favorable Preliminary Dose Expansion Data for Solnerstotug in PD-(L)1 Resistant Tumors

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– Initial clinical activity in a PD-(L)1 resistant population, with an ORR almost three times higher than historical PD-(L)1 rechallenge response rates, with data still maturing –

– One durable complete response in a Merkel Cell Carcinoma (MCC) patient and two partial responses (PR), including one in a second MCC patient and one in a microsatellite instability-high (MSI-H) Colorectal Cancer (CRC) patient, all of whom were previously treated with and progressed on immunotherapy –

– All PD-(L)1 resistant "hot" tumor patients with tumor shrinkage remain on study, suggesting potential for deepening responses over time –

– Sensei to host investor webcast today at 5:30 p.m. ET –

BOSTON, March 27, 2025 (GLOBE NEWSWIRE) -- Sensei Biotherapeutics, Inc. (Nasdaq: SNSE), a clinical-stage biotechnology company focused on the discovery and development of next-generation therapeutics for cancer patients, today announced initial results from the dose expansion portion of its Phase 1/2 trial evaluating solnerstotug (formerly SNS-101), a conditionally active monoclonal antibody targeting VISTA (V-domain Ig suppressor of T cell activation).

"Checkpoint inhibitor resistance remains a significant challenge for patients with advanced cancer, with limited treatment options beyond chemotherapy or clinical trials," said Ron Weitzman, M.D., Chief Medical Officer of Sensei Biotherapeutics. "Historically, patients who progress on PD-(L)1 therapy are estimated to have a ≤5% likelihood of response to PD-(L)1 rechallenge, making this an extremely difficult-to-treat population, and a large unmet medical need. The initial 14% response rate seen with solnerstotug is nearly three times higher than what would typically be expected in this setting. We believe these early data suggest solnerstotug may provide a meaningful clinical benefit in select tumor types, and we look forward to further evaluating its potential in Phase 2."

Phase 1 Dose Expansion Preliminary Results

The Phase 1 dose expansion trial is a multi-center, open-label, dose expansion study evaluating solnerstotug as monotherapy and in combination with Libtayo® (cemiplimab), Regeneron's PD-1 inhibitor, in both a basket of **"hot" tumors** that typically respond to immunotherapy but have progressed on prior PD-(L)1 therapy and a single **"cold" tumor histology (microsatellite stable (MSS) CRC)** that is typically unresponsive to immunotherapy.

As of **March 17, 2025,** the study has enrolled **60 patients**, including:

- 40 patients with "hot" tumors, including Non-Small Cell Lung Cancer (NSCLC), Head and Neck (H&N) cancer, Melanoma, Renal Cell Carcinoma (RCC), Merkel Cell Carcinoma (MCC), MSI-H Colorectal Cancer (CRC), and other tumor types. All patients received the combination of solnerstotug (3 mg/kg or 15 mg/kg) and cemiplimab.
    - At the time of this data cut, 21 "hot" tumor PD-(L)1 resistant patients were considered evaluable for efficacy, having received at least one post-baseline scan. An additional 11 patients have not yet reached the first baseline scan, and an additional 8 patients discontinued the study prior to any post-baseline scan.
- 20 patients with PD-(L)1 non-responsive microsatellite stable (MSS) Colorectal Cancer (CRC) were included to assess potential activity in "cold" tumors. Of these patients, 10 were enrolled in a monotherapy (15 mg/kg) cohort and 10 received the combination of solnerstotug (15 mg/kg) and cemiplimab.
    - 17 MSS CRC patients were considered evaluable for efficacy, having received at least one post-baseline scan. Three patients discontinued the study prior to any post-baseline scan.

Key findings include:

- 14% ORR (3 patients) and 62% DCR (disease control rate) (13 patients) among 21 evaluable PD-(L)1 resistant "hot" tumor patients.
    - Durable complete response (CR) in a MCC patient treated with 15 mg/kg solnerstotug + cemiplimab. Patient continues on treatment at 42+ weeks. Previously received a PD-(L)1 therapy for 15 months in the adjuvant setting

prior to progressing on therapy.
    - Partial response (PR) at Week 12 in a MCC patient treated with 15 mg/kg solnerstotug + cemiplimab. Patient continues on treatment at 12+ weeks. Previously received several lines of checkpoint therapy, including the combination of PD-1 and CTLA-4, with a best response of stable disease prior to progressing on therapy.
    - Partial response (PR) at Week 36 in an MSI-H CRC patient treated with 15 mg/kg solnerstotug + cemiplimab. Patient had durable stable disease (SD) through the course of treatment before converting to a PR at Week 36. Patient continues on treatment at 36+ weeks. Previously received a PD-(L)1 therapy for more than 4 years, where the patient achieved a CR prior to progressing on therapy.
- Six PD-(L)1 resistant patients with SD remain on treatment past 12+ weeks, with tumor reductions ranging from 0% to 17%, suggesting durable disease control in a subset of patients.
- All PD-(L)1 resistant patients on study with tumor shrinkage remain on treatment, suggesting potential for prolonged benefit.
- None of the MSS CRC patients experienced a CR or PR, consistent with prior checkpoint therapy in this “cold” tumor type.

Solnerstotug continues to be well tolerated, with no dose-limiting toxicities and the majority of AEs Grade 1 or 2 in severity. Out of 60 patients, there have been four (7%) cases of Grade 1 cytokine release syndrome (CRS), all mild and manageable. Two patients in the combination cohort experienced immune-mediated events.

A Challenging Treatment Landscape for PD-(L)1 Resistant Tumors

Patients who progress following treatment with PD-1 or PD-L1 inhibitors (“secondary resistance”) face a particularly poor prognosis, as resistance to immune checkpoint blockade is a significant challenge in oncology. According to the Society for Immunotherapy of Cancer (SITC), secondary resistance is defined as disease progression following an initial period of disease control. For patients who develop secondary resistance after treatment with PD-(L)1 immune checkpoint inhibitors, the likelihood of benefiting from a rechallenge with the same therapy is estimated to be **5% or less**.[1] Currently, treatment options for PD-(L)1 resistant tumors are limited, with many patients receiving chemotherapy, experimental therapies in clinical trials, or palliative care in the absence of effective alternatives. Existing immune checkpoint inhibitor (ICI) combination therapies have not been approved in this setting. They are either highly toxic, such as CTLA-4+PD-1 in which up to 40% of patients discontinue due to severe immune-related adverse events (irAEs), or offer limited treatment potential, such as LAG-3+PD-1 where the ORR has been 9-12%.

"While we remain in the early stages of evaluating solnerstotug’s therapeutic potential, the observed responses—particularly in MCC and MSI-H CRC—are encouraging given the historically poor prognosis of these patients once they have progressed on checkpoint therapy,” said Dr. Shiraj Sen, **M.D., Medical Oncologist and Director of Clinical Research at NEXT Oncology - Dallas, and a Principal Investigator for the solnerstotug study**. “Continued clinical evaluation will be key in determining which patients are most likely to benefit from this approach.”

Next Steps: Preparing for Phase 2

Subject to raising sufficient capital, Sensei plans to initiate a **Phase 2 study** in **Q1 2026**, with the trial design and patient selection strategies to be informed by the ongoing dose expansion results. Further analyses, including biomarker-based patient selection, are underway to optimize the Phase 2 design.

Investor Webcast Information

Sensei will host an investor webcast today at 5:30 p.m. ET, featuring company leadership and Dr. Shiraj Sen, M.D., Ph.D., Medical Oncologist and Director of Clinical Research at NEXT Oncology-Dallas, an investigator in the Phase 1/2 study.

Access the live event here: https://lifescievents.com/event/sensei-bio-2/

A replay will be available after the webcast on the Investor Relations page of Sensei’s website: https://investors.senseibio.com

About Sensei Biotherapeutics

Sensei Biotherapeutics (Nasdaq: SNSE) is a clinical-stage biotechnology company developing next-generation immunotherapies for cancer. Through its TMAb™ (Tumor Microenvironment Activated biologics) platform, Sensei engineers conditionally active therapeutics designed to modulate immune responses within the tumor microenvironment. The company’s lead product candidate, solnerstotug, is a VISTA-targeting monoclonal antibody designed to restore T cell activity in checkpoint inhibitor-resistant tumors. For more information, visit www.senseibio.com and follow Sensei on X @SenseiBio and LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

Any statements contained in this press release that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements may be identified by words and phrases such as “believe”, “designed to,” “expect”, “may”, “plan”, “potential”, “will”, and similar expressions, and are based on Sensei’s current beliefs and expectations. These forward-looking statements include expectations regarding the development and potential therapeutic benefits of Sensei’s product candidates, the timing of Sensei’s Phase 1/2 clinical trial of solnerstotug (SNS-101), including reporting of data therefrom, and its plans to initiate a Phase 2 study in the first quarter of 2026, subject to raising sufficient capital. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Risks and uncertainties that may cause actual results to differ materially include uncertainties inherent in the development of therapeutic product candidates, such as the risk that any one or more of Sensei’s product candidates will not be successfully developed or commercialized; the risk of delay or cessation of any planned clinical trials of Sensei’s product candidates; the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical studies and clinical trials, will not be replicated or will not continue in ongoing or future studies or clinical trials involving Sensei’s product candidates; the risk that Sensei’s product candidates or procedures in connection with the administration thereof will not have the safety or efficacy profile that Sensei anticipates; risks associated with Sensei’s dependence on third-party suppliers and manufacturers, including sole source suppliers, over which Sensei may not always have full control; risks regarding the

accuracy of Sensei's estimates of expenses, capital requirements and needs for additional financing; and other risks and uncertainties that are described in Sensei's Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission (SEC) on November 14, 2024 and Sensei's other Periodic Reports filed with the SEC. Any forward-looking statements speak only as of the date of this press release and are based on information available to Sensei as of the date of this release, and Sensei assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.

1. Kluger H, et al. J immunother Cancer 2023

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