NEWS RELEASE

AVENZO THERAPEUTICS PRESENTS INITIAL RESULTS FROM THE PHASE 1/2 STUDY OF AVZO-021, A POTENTIAL BEST-IN-CLASS CDK2 INHIBITOR, AT THE 2025 SAN ANTONIO BREAST CANCER SYMPOSIUM

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SAN DIEGO, Calif. – Dec. 11, 2025 – Avenzo Therapeutics, Inc. ("Avenzo"), a clinical-stage biotechnology company developing next-generation oncology therapies, today reported initial clinical data from the Phase 1 portion of its ongoing Phase 1/2 clinical study of AVZO-021, its potential best-in-class cyclin-dependent kinase 2 (CDK2) selective inhibitor. The initial data highlighted preliminary clinical activity, including objective responses across patients with hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) breast cancer and cyclin E1 (CCNE1)-amplified ovarian cancer. AVZO-021 was generally well tolerated with relatively low incidence and severity of gastrointestinal and hematologic adverse events, which are commonly observed adverse events associated with other CDK inhibitors.

The findings were reported at the 2025 San Antonio Breast Cancer Symposium.

"CDK2 has emerged as an important resistance mechanism in patients with HR+/HER2- breast cancer, especially for patients who progress on CDK4/6 inhibitors," said Alberto J. Montero, M.D., MBA, Clinical Director, Breast Cancer Medical Oncology Program and Diana Hyland Endowed Chair for Breast Cancer at University Hospitals Seidman Cancer Center, Case Western Reserve University. "These data reported today for AVZO-021 are exciting as they not only demonstrate the activity and tolerability of AVZO-021, but the potential for its use in combination with other agents."

AVZO-021, Phase 1 Initial Clinical Data

Utilizing an October 10, 2025 data cut-off date, 35 patients with advanced solid tumors were treated with AVZO-021 monotherapy across nine dose levels, and 10 patients with HR+/HER2- breast cancer were treated with AVZO-021 in combination with fulvestrant across two AVZO-021 dose levels.

The median number of prior therapies in the metastatic setting was 3.0 (range zero to 11), with all patients with HR+/HER2- breast cancer having received at least one prior CDK4/6 inhibitor.

Efficacy-evaluable patients included 19 patients with HR+/HER2- breast cancer or CCNE1-amplified solid tumors treated with AVZO-021 monotherapy doses of 150 mg once daily (QD) and above with at least one post-baseline scan, and nine patients with HR+/HER2- breast cancer treated with AVZO-021 in combination with fulvestrant with at least one post-baseline scan.

As of the October 10, 2025 data cut-off date:

Initial Safety Results

- A total of 45 patients comprise the safety population, including 35 patients with advanced solid tumors treated with AVZO-021 monotherapy at dose levels from 20 mg QD to 250 mg QD, and 10 patients with HR+/HER2- breast cancer treated with AVZO-021 in combination with fulvestrant at AVZO-021 dose levels of 150 mg QD and 200 mg QD.
- All-grade treatment emergent adverse events (TEAEs) reported in greater than 20 percent of patients were nausea (44%), fatigue (38%), anemia (33%), and vomiting (29%).
- The majority of TEAEs were Grade 1 or Grade 2, and no patients had TEAEs leading to treatment discontinuation.

Initial Pharmacokinetic and Pharmacodynamic Results

- PK data suggested continuous CDK2 target coverage was achieved at doses of 90 mg QD and above.
- Comparable exposures of AVZO-021 were observed between AVZO-021 monotherapy and in combination with fulvestrant at 150 mg QD, indicating no drug-drug interaction.
- Significant decreases in circulating tumor DNA (ctDNA) were observed.

Initial Efficacy Results

- Of 19 efficacy-evaluable patients treated with AVZO-021 monotherapy, three patients experienced confirmed responses, including two with HR+/HER2- breast cancer with onset at weeks 15 and 36 and one with CCNE1-amplified ovarian cancer with onset at week 35. Seven patients, who remain on treatment, achieved stable disease, including six with HR+/HER2- breast cancer.

- Of nine efficacy evaluable HR+/HER2- breast cancer patients treated with AVZO-021 in combination with fulvestrant, one patient experienced a confirmed response, with onset at week 7; the confirmatory scan was obtained after the data cut-off date. Three patients, who remain on treatment, achieved stable disease.
- All responders remain on treatment with two on treatment for greater than 48 weeks.

“We are encouraged by the initial safety and efficacy data from this study, especially given multiple patients show improvement over time and remain on treatment,” said Mohammad Hirmand, M.D., Co-founder and Chief Medical Officer of Avenzo Therapeutics. “We look forward to advancing the development of AVZO-021 in combination with our highly potent and selective CDK4 inhibitor, AVZO-023.”

In addition, the company presented the study design for the ongoing Phase 1/2 study evaluating AVZO-023, its potential best-in-class cyclin-dependent kinase 4 (CDK4) selective inhibitor, as a single agent and in combination with AVZO-021 and/or endocrine therapy at the 2025 San Antonio Breast Cancer Symposium.

About Avenzo Therapeutics

Avenzo Therapeutics is a clinical-stage biotechnology company focused on developing next-generation oncology therapies for patients. The company’s pipeline includes potential best-in-class small molecules and antibody-drug conjugates (ADCs). Avenzo’s small molecule inhibitors, AVZO-021 and AVZO-023, are novel, highly potent and selective inhibitors of CDK2 and CDK4, respectively, which are key enzymes involved in cell cycle regulation. AVZO-021, the company’s lead drug candidate, is being studied in a Phase 1/2 study for the treatment of advanced solid tumors and in combinations in HR+/HER2- metastatic breast cancer. AVZO-023 is being studied in a Phase 1/2 study for the treatment of advanced solid tumors and in combinations in HR+/HER2- metastatic breast cancer. Avenzo’s first ADC drug candidate, AVZO-1418, is a potential best-in-class, EGFR/HER3 bispecific ADC that is being studied in a Phase 1/2 study for the treatment of advanced solid tumors. Avenzo’s second ADC drug candidate, AVZO-103, is a potential best-in-class, Nectin4/TROP2 bispecific ADC that is being studied in a Phase 1/2 study for the treatment of advanced solid tumors. Avenzo is headquartered in San Diego, California. For more information, visit us at **www.avenzotx.com** or on **LinkedIn**.

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