NEWS RELEASE

# Avenzo Therapeutics Announces Preliminary Phase 1 Results from the ORION-1 Study of AVZO-023, a Potentially Best-in-Class Selective CDK4 Inhibitor, to Be Presented at the 2026 San Antonio Breast Cancer Symposium

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Preliminary efficacy signal with a 27% ORR in heavily pretreated patients (median of four prior lines of systemic therapy) with HR+/HER2- advanced breast cancer

Strong clinical activity observed at 100 mg BID (50% ORR, 4 of 8 patients), with all responders remaining on treatment

Potentially differentiated safety profile with a low incidence of diarrhea (9% Grade 1/2, no Grade 3/4) and manageable hematologic toxicity, especially at 100 mg BID (22% Grade 1/2 and 11% Grade 3/4 neutrophil count decreased)

Global expansion of the development program ongoing to pursue doublet (AVZO-023 plus endocrine therapy) and triplet (AVZO-023 plus AVZO-021, a potentially best-in-class selective CDK2 inhibitor, plus endocrine therapy) combinations

SAN DIEGO, Calif.--(BUSINESS WIRE)-- **Avenzo Therapeutics, Inc.** (“Avenzo”) (Nasdaq: AVZO), a clinical-stage biotechnology company developing next-generation oncology therapies, today announced preliminary data from the Phase 1 portion of the Phase 1/2 ORION-1 study of AVZO-023, a potentially best-in-class oral selective cyclin-dependent kinase 4 (CDK4) inhibitor, in combination with fulvestrant in patients with hormone receptor-positive,

human epidermal growth factor receptor 2-negative (HR+/HER2-) advanced breast cancer. In 15 efficacy-evaluable, heavily pretreated patients (median of four prior lines of systemic therapy), the objective response rate (ORR) was 27%. At the 100 mg twice-daily (BID) dose level, the ORR was 50% (4 of 8 patients), with all responders remaining on treatment as of the data cutoff. AVZO-023 was observed to be generally well tolerated at doses up to 150 mg BID. The data were released on the SABCS conference portal on November 23, 2026, and will be presented as a poster (Abstract 2618; Presentation Number P1-4-13) at the 2026 San Antonio Breast Cancer Symposium (SABCS) in San Antonio, Texas, on December 9, 2026, from 12:30 p.m. to 2:00 p.m. CT.

“Patients with HR+/HER2- advanced breast cancer who have progressed on CDK4/6 inhibitors have limited treatment options, and there is a clear need for new approaches,” said Timothy A. Yap, M.B.B.S., Ph.D., F.R.C.P., Principal Investigator and presenting author, The University of Texas MD Anderson Cancer Center. “I am encouraged by these data for AVZO-023, which show a preliminary efficacy signal in a heavily pretreated population. The safety profile also appears favorable, including a low incidence of diarrhea, which is important for patients' quality of life as well as their ability to stay on treatment over time.”

**Clinical Data for ORION-1, Phase 1/2 Study of AVZO-023**

As of the October 23, 2026 data cutoff, 23 patients (21 with HR+/HER2- advanced breast cancer who received AVZO-023 plus fulvestrant and two with colorectal cancer who received AVZO-023 monotherapy) were treated in the Part 1A dose-escalation and backfill portion of the study at doses of 25 to 150 mg BID. Median follow-up was 24.1 weeks.

Patients with HR+/HER2- advanced breast cancer were heavily pretreated, with a median of four prior lines of systemic therapy in the advanced or metastatic setting (range 1 to 10). Of these patients, 95% had received a prior CDK4/6 inhibitor and 67% had received prior chemotherapy.

**Preliminary Safety Results**

The overall safety population included 23 patients treated with AVZO-023: five patients at 25 to 75 mg BID, nine at 100 mg BID, and nine at 150 mg BID. AVZO-023 was observed to be generally well tolerated at doses up to 150 mg BID.

- The majority of treatment-emergent adverse events (TEAEs) were Grade 1 or 2; no dose-limiting toxicities (DLTs) were observed at 150 mg BID and one DLT of Grade 3 neutrophil count decreased was observed at 100 mg BID.
- Gastrointestinal toxicity was minimal, with Grade 1/2 diarrhea in 9% of patients and no Grade 3/4 diarrhea.
- Neutrophil count decreased was the most common TEAE (48% overall) with higher incidence seen at 150 mg BID. At 100 mg BID, it was observed in 33% of patients (22% Grade 1/2; 11% Grade 3/4).

- Grade 3/4 treatment-related adverse events (TRAEs) were observed in 22% of patients. TRAEs led to dose reduction in 13% of patients and none led to treatment discontinuation.

**Preliminary PK/PD Results**

Mean half-life was approximately 10 hours. Continuous CDK4 target coverage and thymidine kinase 1 (TK1) reductions were observed at 100 mg BID and higher.

**Preliminary Efficacy Results**

The efficacy-evaluable population (n=15) included patients treated at 100 mg BID or higher with measurable disease at baseline and at least one evaluable post-baseline scan. Responses were investigator-assessed per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1; the ORR included three confirmed partial responses (PRs) and one unconfirmed PR awaiting confirmatory scans.

- The ORR in the study was 27% (4 of 15 patients; 95% confidence interval (CI), 7.8%–55.1%) and all responders were at the 100 mg BID dose level. The disease control rate was 73% (11 of 15 patients; 95% CI, 44.9%–92.2%), with tumor reduction in 67% of patients (10 of 15).
- At 100 mg BID, ORR was 50% (4 of 8 patients), with all responders remaining on treatment as of the data cutoff.
- Multiple patients had deepening tumor reduction over time.
- Median duration of treatment was 16.7 weeks (Min, Max: 6.0, 46.4+). Ten of 15 patients remained on treatment; six had been on treatment for 24 weeks or longer.

“We are very excited by these preliminary data, which we believe support the continued development of AVZO-023 as a potential new option for patients with HR+/HER2- advanced breast cancer who have progressed on CDK4/6 inhibitors,” said Mohammad Hirmand, M.D., Co-founder and Chief Medical Officer of Avenzo Therapeutics. “AVZO-023 also showed a potentially differentiated safety profile, with low gastrointestinal toxicity, especially diarrhea, and manageable hematologic toxicity. We are encouraged by these results and are advancing AVZO-023 through global expansion to pursue both doublet and triplet combinations.”

**About AVZO-023**

AVZO-023 is a highly potent and selective cyclin-dependent kinase 4 (CDK4) inhibitor with best-in-class potential (59-fold CDK4/CDK6 selectivity in preclinical studies) in development for HR+/HER2- advanced breast cancer. It is designed to inhibit CDK4/cyclin D-mediated signaling, a central driver of tumor cell proliferation, while sparing CDK6, whose inhibition is associated with hematologic toxicity. This selectivity may support improved tolerability and combination treatment with endocrine therapy and CDK2 inhibition. AVZO-023 is being evaluated in the Phase

1/2 ORION-1 study in combination with endocrine therapy, and in a triplet combination with AVZO-021, a selective CDK2 inhibitor, and endocrine therapy. Avenzo holds exclusive global rights, excluding Greater China, from Allorion Therapeutics to develop, manufacture and commercialize AVZO-023.

**About AVZO-021**

AVZO-021 is a potentially best-in-class, oral, highly potent, and selective cyclin-dependent kinase 2 (CDK2) inhibitor in development for HR+/HER2- advanced or metastatic breast cancer and other solid tumors. It is designed to target the cyclin E/CDK2 pathway, a key mechanism of resistance to CDK4/6 inhibitors. Its high selectivity over CDK1 may limit off-target toxicity and support use in combination regimens. Enrollment is complete in the Phase 1 portion of the study evaluating AVZO-021 as monotherapy and in combination with endocrine therapy. AVZO-021 is also being evaluated in the Phase 1/2 ORION-1 study in a triplet combination with AVZO-023 and endocrine therapy. The triplet is intended to target both a primary driver of tumor proliferation and a key mechanism of resistance to CDK4/6 inhibitors. Avenzo holds exclusive global rights, excluding Greater China, from Allorion Therapeutics to develop, manufacture and commercialize AVZO-021.

**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 potentially differentiated small molecules and bispecific 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 has completed enrollment in a Phase 1 study as monotherapy in advanced solid tumors and in combination with fulvestrant in HR+/HER2- metastatic breast cancer. AVZO-021 and AVZO-023 are being evaluated in the Phase 1/2 ORION-1 study in HR+/HER2- metastatic breast cancer, where AVZO-023 is administered in combination with endocrine therapy, with or without AVZO-021. Avenzo's first ADC drug candidate, AVZO-1418, is a potentially differentiated EGFR/HER3 bispecific ADC that is being studied in the AVENTINE-1 Phase 1/2 study for the treatment of advanced solid tumors. Avenzo's second ADC drug candidate, AVZO-103, is a potentially differentiated Nectin4/TROP2 bispecific ADC that is being studied in the BEACON-1 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**.

**Forward-Looking Statements**

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements include, without limitation, statements regarding the potential therapeutic benefits, clinical activity, safety, tolerability and differentiation of AVZO-023 and AVZO-021; AVZO-023's potential to

be a best-in-class selective CDK4 inhibitor, including the potential benefits of its selectivity for CDK4 over CDK6 and its potential to inhibit CDK4/cyclin D-mediated signaling while sparing CDK6; AVZO-021's potential to be a best-in-class selective CDK2 inhibitor; the potential for AVZO-023 and AVZO-021 to be used with endocrine therapy in doublet and triplet combinations, including the potential to improve tolerability and target tumor proliferation and resistance to CDK4/6 inhibitors; the timing and content of the planned poster presentation at the 2026 SABCS; the development strategy for AVZO-023 and AVZO-021, including global expansion and ongoing and planned evaluation of doublet and triplet combinations; the potential to provide new treatment options for patients; the potential differentiation, therapeutic applications and continued development of Avenzo's oncology pipeline; and other statements that are not historical facts. Forward-looking statements are based on Avenzo's current expectations and assumptions and are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied. These risks and uncertainties include the early-stage nature of Avenzo's clinical programs; the risk that preliminary results from small patient populations may change with additional patients and longer follow-up and may not be predictive of subsequent results; the risk that unconfirmed responses may not be confirmed and that observed responses may not be durable; the risk that additional or more severe adverse events, including dose-limiting toxicities and hematologic toxicities, may emerge; the risk that preclinical findings, selectivity, proposed mechanisms of action, pharmacokinetic or pharmacodynamic findings, or observed clinical activity may not translate into a differentiated safety or efficacy profile or clinical benefit, whether as monotherapy or in combination; delays or difficulties in initiating, enrolling, expanding or completing clinical trials, including combination studies and studies in additional countries; the risk that ongoing or planned trials may not demonstrate adequate safety and efficacy to support continued development or regulatory approval; Avenzo's dependence on collaboration partners and other third parties for development, manufacturing and clinical trial activities; and Avenzo's ability to obtain sufficient funding to advance its product candidates. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties. You should not place undue reliance on these forward-looking statements, which are made only as of the date hereof or as of the dates indicated in the forward-looking statements. Except as required by law, Avenzo expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in its expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

**Avenzo Therapeutics Contacts:**
Annie Chang
Investor Relations
**achang@avenzotx.com**

Carla Taub
Media Relations

**ctaub@avenzotx.com**

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