# AVEO Oncology, an LG Chem company, Announces Phase 3 Renal Cell Carcinoma Clinical Trial (TiNivo-2) Results

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**AVEO, an LG Chem company** ➞
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*– The addition of nivolumab to low dose tivozanib after prior immune checkpoint inhibitor (ICI) is not superior to standard dose tivozanib alone; as a result, the primary endpoint was not met –*

*– Tivozanib monotherapy (control arm) results provide clinically meaningful efficacy and safety data following front-line ICI combinations –*

*– Safety results reinforce tivozanib is well-tolerated –*

*– Data to be submitted to upcoming scientific meeting –*

BOSTON, July 18, 2024 /PRNewswire/ -- AVEO Oncology, an LG Chem company ("AVEO"), announced today that the TiNivo-2 Phase 3 clinical trial in patients with advanced metastatic renal cell carcinoma (RCC) whose tumors had progressed following prior immune checkpoint inhibitor (ICI) treatment did not meet the primary endpoint of increasing progression free survival (PFS) when nivolumab was added to low dose (0.89 mg) FOTIVDA® (tivozanib). Importantly, the clinical trial's control arm using FOTIVDA as monotherapy at the standard dose (1.34 mg) demonstrated a clinically meaningful outcome in median PFS in the second-line following ICI combination therapy. These results build on the prior ICI dataset from the TIVO-3 clinical trial, FOTIVDA's pivotal phase 3 study, and further support the approved use of FOTIVDA as a safe and effective treatment option in relapsed or refractory advanced RCC following two or more prior systemic therapies.

The results from the TiNivo-2 clinical trial are consistent with other recent RCC phase 3 trials in a similar patient population, making this the second phase 3 clinical trial to suggest that there is no clinical benefit derived from rechallenging RCC patients with immunotherapy after receiving ICI beyond progression on previous ICIs.

"The PFS and safety of the FOTIVDA control arm in the second-line following ICI combinations adds to the growing body of evidence of the importance of a highly selective anti-VEGFR TKI therapy as an effective, well-tolerated treatment option for relapsed or refractory RCC patients treated with prior ICI combination therapy," says Michael P. Bailey, AVEO Oncology Chief Executive Officer and President. "While the addition of an ICI to low dose FOTIVDA did not improve PFS outcomes after prior ICI, we consider the control arm data an important, evidence-based and clinically meaningful contribution to the oncology community treating relapsed or refractory advanced RCC following front-line ICI combinations."

Toni Choueiri, M.D., Director of the Lank Center for Genitourinary Oncology, Director of the Kidney Cancer Center at Dana-Farber Cancer Institute, Jerome and Nancy Kohlberg Chair and Professor of Medicine at Harvard Medical School, and lead investigator comments, "The PFS and safety results from the control arm support tivozanib as an effective and well-tolerated treatment option in the second-line following an ICI combination as prior systemic therapy."

The TiNivo-2 clinical trial was designed to evaluate the benefit of adding nivolumab, a PD-1 checkpoint inhibitor, to low dose FOTIVDA versus standard dose FOTIVDA in the second-line following ICI combinations or the third-line setting following prior ICI. The TiNivo-2 clinical trial enrolled patients across clinical sites in North America, Latin America, and Europe. Patients with RCC who progressed after

receiving immunotherapy were randomized to either tivozanib single agent or in combination with nivolumab. The trial's primary outcome was progression free survival; secondary endpoints included overall survival, overall response rate, duration of response, and safety.

Detailed findings are expected to be presented at an upcoming medical meeting.

**TiNivo-2 Clinical Trial Details**

Phase 3 clinical trial designed to evaluate the safety and efficacy of tivozanib in combination with nivolumab, as compared to tivozanib as a monotherapy, in RCC patients whose tumors have progressed following prior immune checkpoint inhibitor therapy, known as the TiNivo-2 trial.

**About FOTIVDA® (tivozanib)**

FOTIVDA® (tivozanib) is an oral, next-generation vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitor (TKI). It is a potent, selective inhibitor of VEGFRs 1, 2, and 3 with a long half-life designed to improve efficacy and tolerability. AVEO received U.S. Food and Drug Administration (FDA) approval for FOTIVDA on March 10, 2021, for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies, based on data from the TIVO-3 trial comparing FOTIVDA to sorafenib. FOTIVDA was approved in August 2017 in the European Union and other countries in the territory of its partner Recordati UK Ltd. for the treatment of adult patients with advanced RCC. FOTIVDA was discovered by Kyowa Kirin.

**IMPORTANT SAFETY INFORMATION**
**WARNINGS AND PRECAUTION**

**Hypertension and Hypertensive Crisis:** Hypertension was reported in 45% of FOTIVDA-treated patients with 22% of the events ≥Grade 3. Hypertensive crises were reported in 0.8% of patients. Do not initiate FOTIVDA in patients with uncontrolled hypertension. Monitor for hypertension and treat as needed. Reduce the FOTIVDA dose for persistent hypertension not controlled by anti-hypertensive medications. Discontinue FOTIVDA for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

**Cardiac Failure:** Cardiac failures were reported in 1.6% of FOTIVDA-treated patients, with 1% of events reported as ≥Grade 3; 0.6% of events were fatal. Monitor for signs or symptoms of cardiac failure throughout treatment with FOTIVDA. Manage with dose interruption, dose reduction, or discontinuation.

**Cardiac Ischemia and Arterial Thromboembolic Events:** Cardiac ischemia in FOTIVDA-treated patients were reported in 3.2%; 0.4% of events were fatal. Arterial thromboembolic events were reported in 2.0% of FOTIVDA-treated patients, including death due to ischemic stroke (0.1%). Closely monitor patients who are at risk for, or who have a history of these events. Discontinue FOTIVDA in patients who develop severe arterial thromboembolic events, such as myocardial infarction and stroke.

**Venous Thrombotic Events:** Venous thromboembolic events were reported in 2.4% of FOTIVDA-treated patients, including 0.3% fatal events. Closely monitor patients who are at increased risk for these events. Discontinue FOTIVDA in patients who develop serious venous thromboembolic events.

**Hemorrhagic Events:** Hemorrhagic events were reported in 11% of FOTIVDA-treated patients; 0.2% of events were fatal. FOTIVDA should be used with caution in patients who are at risk for or who have a history of bleeding.

**Proteinuria:** Proteinuria was reported in 8% of FOTIVDA-treated patients, with 2% Grade 3. Monitor throughout treatment with FOTIVDA. For moderate to severe proteinuria, reduce the dose or interrupt treatment with FOTIVDA. Discontinue FOTIVDA in patients who develop nephrotic syndrome.

**Thyroid Dysfunction:** Thyroid dysfunction events were reported in 11% of FOTIVDA-treated patients, with 0.3% of events reported as ≥Grade 3. Monitor thyroid function before initiation and throughout treatment with FOTIVDA.

**Wound Healing Complications:** Withhold FOTIVDA for at least 24 days prior to elective surgery. Do not administer FOTIVDA for at least 2 weeks after major surgery and until adequate wound healing is observed. The safety of resumption of FOTIVDA after resolution of wound healing complications has not been established.

**Reversible Posterior Leukoencephalopathy Syndrome (RPLS):** RPLS, a syndrome of subcortical vasogenic edema diagnosed by MRI, can occur with FOTIVDA. Evaluate for RPLS in patients presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue FOTIVDA if signs or symptoms of RPLS occur.

**Embryo-fetal Toxicity:** FOTIVDA can cause fetal harm. Advise patients of the potential risk to a fetus, to avoid becoming pregnant and to use contraception during treatment and for one month after the last dose of FOTIVDA. Advise males with female partners of reproductive potential to use effective contraception during treatment and for one month after the last dose of FOTIVDA.

**Allergic Reaction to Tartrazine:** FOTIVDA 0.89 mg capsule contains FD&C Yellow No. 5 (tartrazine) as an imprint ink which may cause allergic-type reactions (including bronchial asthma) in certain susceptible patients.

**ADVERSE REACTIONS**

The most commonly reported (≥20%) adverse reactions were: fatigue/asthenia, hypertension, diarrhea, decreased appetite, nausea, dysphonia, hypothyroidism, cough, and stomatitis. Serious adverse reactions reported in >2% of patients included bleeding (3.5%), venous thromboembolism (3.5%), arterial thromboembolism (2.9%), acute kidney injury (2.3%), and hepatobiliary disorders (2.3%).

**DRUG INTERACTIONS**

**Strong CYP3A4 Inducers:** Avoid coadministration of FOTIVDA with strong CYP3A4 inducers.

**USE IN SPECIFIC POPULATIONS**

**Lactation:** Advise women not to breastfeed during FOTIVDA treatment and for at least 1 month after the last dose.

**Renal Impairment:** The recommended dosage for patients with end-stage renal disease has not been established.

**Hepatic Impairment:** Reduce the FOTIVDA dose for patients with moderate hepatic impairment. The recommended dosage in patients with severe hepatic impairment has not been established.

**To report SUSPECTED ADVERSE REACTIONS, contact AVEO Pharmaceuticals, Inc. at 1-833-FOTIVDA (1-833-368-4832) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

**Please see full Prescribing Information for FOTIVDA® (tivozanib).**

**About AVEO Pharmaceuticals, Inc.**

AVEO is an oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for patients with cancer. AVEO currently markets FOTIVDA® (tivozanib) in the U.S. for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies. AVEO continues to develop FOTIVDA in immuno-oncology and other novel targeted combinations in RCC and other indications, and has other investigational programs in clinical development. AVEO became a wholly owned subsidiary of LG Chem Life Sciences USA, Inc. on January 19, 2023. AVEO continues to operate under the AVEO Oncology, an LG Chem company, name.

**About LG Chem, Ltd. and LG Chem Life Sciences**

LG Chem, Ltd. (LG Chem) is a leading global chemical company with a diversified business portfolio in the key areas of petrochemicals, advanced materials, and life sciences. The company manufactures a wide range of products from high-value added petrochemicals to renewable plastics, specializing in cutting-edge electronic and battery materials, as well as drugs and vaccines to deliver differentiated solutions for its customers. LG Chem Life Sciences develops, manufactures, and globally commercializes pharmaceutical products, with a focus on Oncology, Immunology, and Metabolic diseases. Our mission is to transform people's lives through inspiring science and leading innovation. For more information, please visit **www.lgchem.com**.

**References**


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3. OPDIVO (nivolumab)[https://packageinserts.bms.com/pi/pi_opdivo.pdf ].Princeton, NJ: Bristol-Myers Squibb Company.


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