Aravive Receives IND Clearance for Phase 1b/Phase 2 Clinical Trial of AVB-500 in Patients with Clear Cell Renal Cell Carcinoma

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HOUSTON, Jan. 13, 2020 (GLOBE NEWSWIRE) -- Aravive, Inc. (Nasdaq: ARAV), a clinical-stage biopharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) has cleared the company's Investigational New Drug (IND) application for investigation of the company's lead candidate, AVB-500, for the treatment of clear cell renal cell carcinoma (ccRCC).

"The rapidly changing landscape of front line metastatic ccRCC has created a clinical need for studies in the second-line setting," said Brian Rini, M.D, Ingram Professor of Medicine, Vanderbilt-Ingram Cancer Center (VICC), Nashville, TN. "Investigation into the role of AXL in RCC to build on VEGF inhibition in this setting is an exciting new frontier in RCC research."

"Preclinical data demonstrate that inactivation of AXL/GAS6 pathway via treatment with AVB-500 in ccRCC cells plays a key role in both anti-tumor and anti-metastatic effects," said Gail Mcintyre, Ph.D., chief scientific officer of Aravive.

The study has a Phase 1b safety portion and a Phase 2 randomized, controlled portion. The Phase 1b portion will investigate the safety and tolerability of escalating doses of AVB-500 in combination with cabozantanib in patients with advanced clear cell renal cell carcinoma that have progressed with or were intolerant to front-line treatment. The primary endpoints for the Phase 1b portion of the clinical trial are safety, pharmacokinetic and pharmacodynamic measurements with secondary endpoints including preliminary activity measures. The Phase 2 portion of the study will investigate the recommended AVB-500 dose identified during the Phase 1b portion in combination with cabozantinib versus cabozantinib alone in patients with advanced clear cell renal cell carcinoma that have progressed with or were intolerant to front-line treatment. The primary endpoint will be progression free survival. The clinical trial will also explore AVB-500 effects on biomarkers (GAS6) in serum.

About ccRCC
Kidney cancer is a leading cause of cancer-related deaths in the United States and is among the 10 most common cancers in both men and women. Metastasis to distant organs including the lung, bone, liver and brain is the primary cause of death in kidney cancer patients as only 12% of metastatic kidney cancer will survive past 5 years. According to the American Cancer Society, it is estimated that there will be approximately 73,750 new cases of kidney cancer in the U.S. and 14,830 people will die from this disease in 2020.

Preclinical studies have demonstrated there is a molecular link between the tumor suppressor gene VHL that is mutated in more than 80% of ccRCC tumors and AXL expression in RCC. The expression of the receptor tyrosine kinase AXL in tumors has been postulated as a biomarker and increased mRNA levels of AXL is associated with poor prognosis in renal cell cancer.

About AVB-500
AVB-500 is a therapeutic recombinant fusion protein that has been shown to neutralize GAS6 activity by binding to GAS6 with very high affinity. In doing so, AVB-500 selectively inhibits the GAS6-AXL signaling pathway. In preclinical studies, GAS6-AXL inhibition has shown anti-tumor activity, both as a single agent and in combination with a variety of anticancer therapies including radiation therapy, immuno-oncology agents and chemotherapeutic drugs that affect DNA replication and repair. Increased expression of AXL and GAS6 in tumors is correlated to poor prognosis and survival, and has been implicated in therapeutic resistance to conventional chemotherapeutics and targeted therapies.

Aravive reported positive data from the expansion cohort in the Phase 1b portion of a Phase 1b/2 clinical trial of AVB-500 in platinum-resistant recurrent ovarian cancer. An investigator-sponsored Phase 1 study of AVB-500, in combination with durvalumab in patients with platinum-resistant recurrent epithelial ovarian cancer, is also ongoing. A Phase 2a trial in renal fibrosis initiated late 2019. Based on AVB-500's safety profile and specifically targeted mechanism of action, this drug candidate has the potential to be used both in combination with existing therapies, as well as a maintenance drug. The U.S. Food and Drug Administration granted Fast Track Designation to AVB-500 in platinum-resistant recurrent ovarian cancer.

About Aravive
Aravive, Inc. (Nasdaq: ARAV) is a clinical-stage biopharmaceutical company developing treatments designed to halt the progression of life-threatening diseases, including cancer and fibrosis. Aravive's lead product candidate, AVB-500, is an ultra-high affinity decoy protein that targets the GAS6-AXL signaling pathway. By capturing serum GAS6, AVB-500 starves the AXL pathway of its signal, potentially halting the biological programming that promotes disease progression. AXL receptor signaling plays an important role in multiple types of malignancies by promoting metastasis, cancer cell survival, resistance to treatments, and immune suppression. The GAS6-AXL signaling pathway also plays a significant role in fibrogenesis. Aravive is evaluating AVB-500 in platinum-resistant ovarian cancer and kidney fibrosis and intends to expand development into additional oncology and fibrotic indications. Aravive is based in Houston, Texas and received a Product Development Award from the Cancer Prevention & Research Institute of Texas (CPRIT) in 2016. For more information, please visit www.aravive.com.

Forward-Looking Statements
This communication contains forward-looking statements (including within the meaning of Section 21E of the United States Securities Exchange Act of 1934, as amended, and Section 27A of the United States Securities Act of 1933, as amended), express or implied, concerning the potential of AVB-500 to be used both in combination with existing therapies, as well as a maintenance drug, the potential of AVB-500 to halt the biological programming that promotes disease progression and the expansion of the development of AVB-500 into additional oncology and fibrotic indications. Forward-looking statements are based on current beliefs and assumptions, are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results to differ materially from those contained in any forward-looking statement as a result of various factors, including, but not limited to, risks and uncertainties related to: the Company's ability to expand development in 2020 into additional oncology and fibrotic indications, the Company's dependence upon AVB-500, AVB-500's ability to have favorable results in clinical trials and results that are as

favorable as those of preclinical studies, the ability to receive regulatory approval, potential delays in the Company's clinical trials due to regulatory requirements or difficulty identifying qualified investigators or enrolling patients; the risk that AVB-500 may cause serious side effects or have properties that delay or prevent regulatory approval or limit its commercial potential; the risk that the Company may encounter difficulties in manufacturing AVB-500; if AVB-500 is approved, risks associated with its market acceptance, including pricing and reimbursement; potential difficulties enforcing the Company's intellectual property rights; the Company's reliance on its licensor of intellectual property and financing needs. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors included in the Company's Annual Report on Form 10-K and Form 10-K/A for the fiscal year ended December 31, 2018, recent Current Reports on Form 8-K and subsequent filings with the SEC. Except as required by applicable law, the Company undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.

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