Aravive Announces Publication of AVB-500 Nonclinical Study in Treatment-Resistant ccRCC Animal Models in Cancer Research

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AVB-500 reduced tumor size and blood vessel density in animal models

Study highlights role of GAS6/AXL signaling in promoting tumor angiogenesis through regulation of plasminogen receptor S100A10

Data supports Aravive's clinical development plan in clear cell renal cell carcinoma (ccRCC)

HOUSTON, Oct. 18, 2019 (GLOBE NEWSWIRE) -- Aravive, Inc. (Nasdaq: ARAV), a clinical-stage biopharmaceutical company developing treatments designed to halt the progression of life-threatening diseases, including cancer and fibrosis, today announced publication of data from a nonclinical study of AVB-500, the company's lead product candidate, which demonstrated reduction in tumor size and blood vessel density in animal models of clear cell renal cell carcinoma (ccRCC). The research elucidates the role of GAS6/AXL signaling in promoting tumor angiogenesis through control of plasminogen receptor S100A10. The study, entitled "S100A10 is a critical mediator of GAS6/AXL-induced angiogenesis in renal cell carcinoma" was published in the October edition of the peer-reviewed journal *Cancer Research*.

"This study has important therapeutic implications, suggesting that an anti-GAS6 therapy may be a potentially effective approach to prevent and treat tyrosine kinase inhibitor (TKI)-resistant disease, supporting the rationale for combining AVB-500 with antiangiogenic agents in the treatment of advanced kidney cancer," said Gail McIntyre, Ph.D., chief scientific officer of Aravive. "The research supports our plans to develop AVB-500 in ccRCC, and we remain on track to initiate clinical development in 4Q2019/1Q2020."

Key conclusions of the study include:

- Genetic inhibition of AXL in ccRCC cells reduces tumor vessel density and growth.
- GAS6/AXL signaling promotes S100A10 expression in ccRCC cells through SRC family kinase activity.
- GAS6 inhibition by AVB-500 synergizes with pazopanib and axitinib to reduce ccRCC patient-derived xenograft growth and vessel density.
- GAS6 inhibition by AVB-500 reduces the growth of a TKI resistant ccRCC patient-derived xenograft.

About Clear Cell Renal Cell Carcinoma

Clear cell renal cell carcinoma (ccRCC) is the most common type of kidney cancer and has been increasing in prevalence in the U.S. and Europe over the last several decades. As many as 25 percent of patients already have metastatic disease at the time of diagnosis. ccRCC tumors are highly vascularized and initially respond to antiangiogenic therapies, including tyrosine kinase inhibitors. While antiangiogenic therapy has significantly increased progression-free survival in people with advanced renal cancer, the majority of individuals treated with these agents eventually become resistant and progress.

About AVB-500

AVB-500 (previously called AVB-S6-500) 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 or 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 is currently enrolling 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-studied Phase 1 study of AVB-500 in combination with durvalumab in patients with platinum-resistant, recurrent epithelial ovarian cancer is also ongoing. A Phase 1 clinical trial in healthy volunteers (NCT03401528) investigating the safety, pharmacokinetics, and pharmacodynamics of AVB-500 met the safety and tolerability endpoints and demonstrated clinical proof-of-mechanism for AVB-500 in neutralizing GAS6. Based on AVB-500's favorable safety profile, coupled with its specifically targeted mechanism of action, the protein has the potential to be used both in combination with existing therapies, as well as a maintenance drug. U.S. FDA granted Fast Track Designation to Aravive Biologics' AVB-500 in platinum-resistant recurrent ovarian cancer in 2018.

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 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. Aravive was one of FierceBiotech's Fierce 15 in 2017. 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 Company's goals, intentions and expectations as to future plans or events, including statements regarding the suggestion that GAS6 therapy may be a potentially effective approach to prevent and treat tyrosine kinase inhibitor (TKI)-resistant disease, supporting the rationale for combining AVB-500 with antiangiogenic agents in the treatment of advanced kidney cancer, plans to develop AVB-500 in ccRCC, remaining on track to initiate clinical development in 4Q2019/1Q2020, the potential of AVB-500 to be used both in combination with existing therapies, as well as a maintenance drug 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 into additional oncology and fibrotic indications, the Company's dependence upon AVB-500, AVB-500's ability to have favorable results in clinical trials or 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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