Aravive Announces Successful Completion of Phase 1b Trial Evaluating AVB-500 in Platinum Resistant Ovarian Cancer

July 23, 2020

Identifies Recommended Phase 2 Dose for Continued Clinical Development of AVB-500 in Platinum Resistant Ovarian Cancer

Aravive to Host Conference Call and Webcast Today at 8:30 a.m. ET

HOUSTON, July 23, 2020 (GLOBE NEWSWIRE) -- Aravive, Inc. (Nasdaq: ARAV), a clinical-stage oncology company developing transformative therapeutics, today announced the successful completion of the Phase 1b trial of its AVB-500 drug candidate in platinum resistant ovarian cancer (PROC) and selection of the recommended Phase 2 dose (RP2D).

“Aravive is grateful to the patients and their physicians who participated in this trial,” said Gail McIntyre, Ph.D., chief executive officer at Aravive. “We are very encouraged by the potential of AVB-500 to improve responses and progression free survival in combination with chemotherapy in platinum resistant ovarian cancer. The information we have obtained from the clinical data together with some informal preliminary feedback from the FDA have helped inform our Phase 2/3 trial strategy. We look forward to formally discussing these results and our development plan with the FDA by the end of 2020.”

Phase 1b Results
The safety of AVB-500 has been studied in 84 subjects, including 31 healthy volunteers in a Phase 1a trial and 53 patients with PROC in a Phase 1b trial (40 in 10 mg/kg cohort, 6 in 15 mg/kg cohort, and 7 in 20 mg/kg cohort). The primary objective of the PROC trial was to assess safety of AVB-500 in combination with paclitaxel (PAC) or pegylated liposomal doxorubicin (PLD). Secondary endpoints included objective response rate (ORR), CA-125 response, clinical benefit rate, progression free survival (PFS), overall survival, pharmacokinetic (PK) profile, GAS6 serum levels, and anti-drug antibody titers.

Safety Data: Analysis of all safety data to date demonstrates that AVB-500 has been generally well-tolerated with no dose-limiting toxicities or unexpected safety signals. There have been no AVB-500-related SAEs reported to date. There were two types of adverse events that were considered related to AVB-500, as determined by an independent medical monitor: infusion reactions and fatigue. A premedication regimen was designed and implemented during the trial to manage potential infusion reactions.

Pharmacokinetics: Prior data analysis of 31 patients from the 10 mg/kg cohort showed that blood trough levels of AVB-500 demonstrated statistically significant correlation with clinical activity, as patients who achieved minimal efficacious concentration (MEC) >13.8 mg/L demonstrated a greater likelihood of response and prolonged PFS. Updated modeling using actual data from all enrolled patients demonstrated that 59%, 84%, and 93% of patients achieved MEC at doses of 10 mg/kg, 15 mg/kg, and 20 mg/kg, respectively. Furthermore, at 20 mg/kg, a large percentage of subjects is projected to have trough levels greater than 4 times the MEC. These data suggest that at 15 mg/kg, the pharmacokinetics of AVB-500 start to plateau and support the choice of 15 mg/kg as RP2D for AVB-500.

Preliminary Efficacy: While the Phase 1b trial was a safety trial and not powered to demonstrate efficacy, the investigator-assessed best response (RECIST V1.1) to AVB-500 across all cohorts supports promising clinical activity:

10 mg/kg cohort, 37 out of 40 patients evaluable:

- 31% ORR (5/16) among those treated with AVB-500 in combination with PAC, with 1 complete response (CR). Patients given AVB-500 plus PAC who achieved MEC of AVB-500 demonstrated improved ORR of 50% (4/8), with 1 CR.
- The PFS among those who achieved MEC of AVB-500 was 7.5 months versus 2.28 months with those below MEC (p=0.0062).
- 21.6% ORR (8/37) in all evaluable patients, regardless of their MEC or use of PAC or PLD.
- All responses have been confirmed.

15 mg/kg cohort, 5 out of 6 patients evaluable:

- All 5 patients in this cohort experienced clinical benefit, with 1 CR (continuing to show CR 3 months after discontinuing chemotherapy while on AVB-500 as single agent), 2 partial responses (PR), and 2 stable disease (SD).
- All responses have been confirmed.

20 mg/kg cohort, 7 out of 7 patients evaluable:

- Of the 7 patients in this cohort, there was 1 PR (with CR of target lesion; not confirmed), 1 SD, and 5 with progressive disease (PD).
- A post-hoc analysis of tumor expression showed that 4 patients whose best response was PD did not express GAS6 (3) and/or had low amounts of AXL (2) on immunohistopathology of their tumors. While they were enrolled per protocol in the

Phase 1b trial, these patients do not appear to be representative of the eventual AVB-500 target population, as they are mostly rare subtypes of PROC and such patients based on their clinical characteristics will not be eligible for the planned Phase 2/3 trial.

Other notable findings:

- AVB-500 plus PAC appeared to perform better than AVB-500 plus PLD.
  - Across all cohorts, AVB-500 plus PAC data show an ORR of 35% (8/23, including 2 CRs) compared to ORR of 15% (4/26) in AVB-500 plus PLD.

- AVB-500 plus chemo appeared to perform better in patients without previous exposure to bevacizumab.
  - In a subgroup analysis of patients who had not been previously exposed to bevacizumab in their prior lines of therapy, AVB-500 yielded an ORR of 60% (6/10 including 2 CR) when combined with PAC and an ORR of 19% (3/16) when combined with PLD. For reference, control arms of the third-party AURELIA Trial of bevacizumab (NCT00976911) showed ORR of 30.2% (out of 55 patients total) with PAC alone and 7.8% (out of 64 patients total) with PLD alone.

- Serum levels of soluble AXL (sAXL)/GAS6 ratio seemed to correlate with response to AVB-500.
  - In the entire Phase 1b cohort, patients with a high sAXL/GAS6 ratio had 30% ORR (10/33) versus 0% ORR (0/15) in patients with a low sAXL/GAS6 ratio. In the PAC cohort, patients with a high sAXL/GAS6 ratio had 43% ORR (6/14) versus 0% ORR (0/7) in patients with a low sAXL/GAS6 ratio. Notably, patients with high sAXL/GAS6 ratio who had not previously received bevacizumab achieved ORR of 71% (5/7).
  - Historically, high sAXL has been associated with a poor prognosis; however, AVB-500 plus PAC or PLD appeared correlated with improved clinical outcomes in this population.
  - Use of serum biomarkers such as sAXL/GAS6 ratio as potential stratification biomarker(s) will be explored in future clinical trials.

“Improved therapeutic approaches, especially targeted therapies, are urgently needed for patients with ovarian cancer who are resistant to standard of care therapy and have limited treatment options,” said Katherine Fuh, M.D., Ph.D., Assistant Professor, Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, Center for Reproductive Health Sciences, Washington University School of Medicine, St. Louis, MO. “AVB-500’s novel mechanism of action has the potential to be combined with any number of anticancer agents, including DNA-damaging agents, PARP inhibitors, bevacizumab as well as immuno-oncology agents and check point inhibitors to change the way we treat ovarian cancer.”

Conference Call Information
Aravive will host a live conference call and webcast at 8:30 a.m. ET today to discuss these clinical data. The conference call may be accessed by dialing (844) 281-9845 (domestic) and (314) 888-4254 (international) and referring to conference ID 6277266. A webcast of the conference call and an accompanying slide presentation will be available in the Investors section of the Aravive website at https://ir.aravive.com. The archived webcast will be available on Aravive’s website after the conference call.

About AVB500-OC-002
Aravive initiated a Phase 1b dose-escalation trial (AVB500-OC-002) evaluating AVB-500 in combination with pegylated liposomal doxorubicin (PLD) or paclitaxel (PAC) for patients with platinum resistant ovarian cancer (PROC) in December 2018. Aravive reported positive preliminary data from the Phase 1b trial at 10 mg/kg in November 2019, demonstrating a relationship between AVB-500 blood levels and anti-tumor response. Additionally, AVB-500 is being studied in Investigator-sponsored Phase 1/2 trials, in combination with durvalumab in patients with platinum-resistant recurrent epithelial ovarian cancer and with avelumab in patients with advanced urothelial Carcinoma (COAXIN).

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 preclinical models. In doing so, AVB-500 selectively inhibits the GAS6-AXL signaling pathway which is upregulated in multiple cancer types including ovarian cancer. In preclinical studies, GAS6-AXL inhibition has shown anti-tumor activity 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 has been correlated with poor prognosis and decreased survival and has been implicated in therapeutic resistance to conventional chemotherapeutics and targeted therapies. AVB-500 is currently being evaluated in clinical trials and has been granted Fast Track Designation by The U.S. Food and Drug Administration (FDA) in platinum-resistant recurrent ovarian cancer.

About Aravive
Aravive, Inc. (Nasdaq: ARAV) is a clinical-stage oncology company developing transformative treatments designed to halt the progression of life-threatening diseases. Aravive’s lead product candidate, AVB-500, is an ultra-high affinity decoy protein that targets the GAS6-AXL signaling pathway. Aravive recently initiated a discovery program to develop a high affinity bispecific program targeting CCN2 (CTGF) for treatment of cancer and fibrosis. 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, such as the potential of AVB-500 to improve responses and progression free survival in combination with chemotherapy in platinum resistant ovarian cancer, the potential of a Phase 2/3 trial, and the potential of combining AVB-500’s novel mechanism of action with other anticancer agents, including DNA-damaging agents, PARP inhibitors, bevacizumab as well as immuno-oncology agents and check point inhibitors to change the way we treat ovarian cancer. 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 show the potential of AVB-500 to improve responses and progression free survival in combination with chemotherapy in platinum resistant ovarian cancer, the Company's ability to successfully combine AVB-500's novel mechanism of action with other anticancer agents, the ability to properly fund the Company, the ability of the new directors and management team to deliver on the Company's strategic vision and execute on its business plan, the impact of COVID-19 on the Company's clinical strategy, clinical trials, supply chain and fundraising, 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, the clinical trials of AVB-500 having results that are as favorable as those of preclinical and clinical trials, 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 especially in light of the COVID-19 pandemic; 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 for the fiscal year ended December 31, 2019, 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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