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New Research Suggests Anti-viral Role for Aravive Biologics' Anti-AXL Candidate Against ZIKA Virus

-- *Cell Reports* publication highlights dual role of Gas6-AXL during ZIKA infection: promoting viral entry of glial cells in the developing brain and modulating innate immune responses to facilitate infection --

-- Aravive-S6 shown *in vitro* to inhibit ZIKA infection of human glial cells, adding potential antiviral uses to the AXL decoy's previously reported anti-cancer properties --

HOUSTON, TX (January 10, 2017): Newly published *in vitro* research reveals that the ability of ZIKA virus (ZIKV) to infect glial cells in the developing brain is mediated by the Gas6-AXL pathway, and that Aravive Biologic's engineered decoy AXL receptor, Aravive-S6 (referred to as MYD1 in the publication) can block ZIKV infection by intercepting Gas6 to prevent AXL signaling. These findings suggest a potential antiviral role for Aravive-S6 in addition to its previously reported anticancer activity.

The new findings were published today in *Cell Reports* by researchers from Inserm (the French national institute of health and medical research), and their collaborators including Aravive Biologics. The publication, entitled "AXL mediates ZIKV entry in human glial cells and modulates innate immune responses," reports that ZIKV entry into cells requires the AXL ligand, Gas6, which bridges the viral particles to glial cells, where the virus is then internalized. During virus entry of the cell, the ZIKV/Gas6 complex activates AXL kinase activity, which dampens the interferon response to the virus and facilitates infection. The researchers also report that ZIKV infection of human glial cells is inhibited by Aravive's engineered AXL decoy receptor, Aravive-S6 (MYD1).

ZIKV is a mosquito-borne flavivirus, and infection with the virus has been linked to several neurological disorders, including Guillain-Barré syndrome, meningoencephalitis and myelitis. Moreover the infection of pregnant women by ZIKV has resulted in fetal abnormalities, congenital microcephaly and abortion. In the developing fetal brain, ZIKV targets neural progenitor cells, alters cell division and induces cell death, hampering brain development. Until now, the mechanism by which ZIKV enters target cells has been poorly understood.

“Our research results highlight the dual role of AXL during ZIKV infection of glial cells, promoting viral entry and modulating innate immune responses against the virus,” said Dr. Ali Amara, Inserm Research Director and Head of the Team - Biology of Emerging Viruses, INSERM U944 CNRS 7212 at the Hospital Saint Louis, Paris. “Therefore, inhibiting AXL function may represent a potential target for future antiviral therapies.”

“Previous research has shown that the ability of Aravive-S6 to block AXL signaling by intercepting and strongly binding Gas6 has potential for the treatment of many cancers, both on its own and in synergistic combination with radiation, chemotherapeutics, PARP inhibitors and checkpoint inhibitors,” said Ray Tabibiazar, M.D., President and Chief Executive Officer of Aravive Biologics. “This new research suggests that Aravive-S6 may also be able to block infection by ZIKV and some related viruses, such as dengue virus, which share methods of cell entry and infection. We look forward to further exploring the antiviral properties of this class of molecules.”

This work was supported by grants from the U.S. National Institutes of Health (NIH, Grant R01 N°AI101400), the Labex IBEID, and the French National Research Agency (ANR) [“Investissements d’Avenir” program ANR-10-IHUB -0002 and CE14-0029 grant TIMTAMDEN]. It was also funded by the ZIKAlliance project, which has received funding from the European Union’s Horizon 2020 research and innovation program under grant agreement No. 734548.

About Aravive-S6

Aravive-S6 is a novel therapeutic candidate that acts as a decoy to bind Gas-6 with high affinity and prevent its triggering of the AXL signaling pathway. Research has shown AXL signaling to be 1) a key “survival switch” that scientists believe promotes tumor growth and metastasis, and resistance to other anticancer agents; and 2) a mechanism by which certain virus, including ZIKV, enter glial cells and modulate immune responses to facilitate viral infection. Preclinical studies have shown both anticancer and antiviral properties for Aravive-S6, including synergies with a variety of anticancer agents: radiation therapy, immuno-oncology agents, and drugs that affect DNA replication and repair, including PARP inhibitors. Aravive Biologics is currently advancing the development of Aravive-S6 in the oncology field with a goal of filing an IND in late 2017 to begin clinical studies in acute myeloid leukemia (AML).

About Aravive Biologics, Inc.

Aravive Biologics is a privately held, late pre-clinical stage biopharmaceutical company developing novel, highly selective cancer therapies that treat serious malignancies while sparing normal healthy cells. The company’s lead program is focused on the GAS6/AXL pathway, where activation appears to play a critical role in multiple types of cancer malignancies by promoting tumor metastasis and cell survival. Aravive Biologics has generated strong preclinical data for its lead drug candidate, Aravive-S6, in both acute myeloid leukemia (AML) and solid tumors including ovarian, pancreatic, and breast cancers. The company is based in Houston, Texas, and receives support from the Cancer Prevention & Research Institute of Texas (CPRIT). For more information, please visit our website at http://www.aravive.com.

Forward Looking Statement

This press release contains forward-looking statements. Forward-looking statements contained in this press release include, without limitation, statements regarding the ability of Aravive-S6 to block ZIKV infection by intercepting Gas6 to prevent AXL signaling, inhibition of AXL function representing a potential target for future antiviral therapies, Aravive-S6 having the potential for the treatment of many cancers, both on its own and in synergistic combination with radiation, chemotherapeutics, PARP inhibitors and checkpoint inhibitors, the suggestion that Aravive-S6 may also be able to block infection by ZIKV and some viruses, such as dengue virus, which share methods of cell entry and infection. Words such as "may," “believe,” "will," "expect," "plan," "anticipate," "estimate," "intend" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These forward-looking statements are not guarantees of future performance and involve a number of unknown risks, assumptions, uncertainties and factors that are beyond Aravive Biologics' control including the ability of Aravive-S6 to block ZIKV infection and other related viruses, and the ability of Aravive-S6 to treat cancer, the ability of Aravive-S6 to demonstrate safety and efficacy, as well as clinical results that are consistent with prior in vitro results, the ability to enroll patients and complete the clinical trials on time and achieve desired results and benefits, the company’s ability to obtain regulatory approvals for commercialization of product candidates or to comply with ongoing regulatory requirements, regulatory limitations relating to the company’s ability to promote or commercialize its product candidates for specific indications, acceptance of its product candidates in the marketplace and the successful development, marketing or sale of products, the company’s ability to maintain its license agreements, the continued maintenance and growth of its patent estate, its ability to establish and maintain collaborations, its ability to obtain or maintain the capital or grants necessary to fund its research and development activities, and its ability to retain its key scientists or management personnel. All forward-looking statements are based on Aravive Biologics' expectations and assumptions as of the date of this press release. Actual results may differ materially from these forward-looking statements. Except as required by law, Aravive Biologics expressly disclaims any responsibility to update any forward-looking statement contained herein, whether as a result of new information, future events or otherwise.

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