Press Release

The Wistar Institute and Jubilant Therapeutics Inc. Find PAD4 Inhibition in Neutrophils, Halts Cancer Progression and Metastasis

Novel PAD4 inhibitor reduces primary tumor, metastases and enhances checkpoint inhibitor treatments

Philadelphia, September 07, 2022 - Researchers in the laboratory of **Yulia Nefedova, M.D., Ph.D.**, at The Wistar Institute and collaborators at the **Jubilant Therapeutics Inc.** have uncovered a novel mechanism by which protein arginine deiminase 4 (PAD4) in neutrophils promotes cancer progression. The paper also found that inhibition of this function of PAD4 reduces primary tumor growth and metastasis and enhances checkpoint inhibitor treatments. Jubilant Therapeutics Inc. is developing a novel small molecule PAD4 inhibitor that directly targets this mechanism. The findings appear in *Cancer Research*, a journal of the American Association for Cancer Research.

"Development of metastases remains a leading cause of death from cancer. Tumor-associated neutrophils have long been implicated in cancer progression. Understanding the mechanisms by which these cells promote tumor growth and metastatic spread is critically important for the development of new treatments," **shares Yulia Nefedova, M.D., Ph.D., associate professor, Immunology, Microenvironment & Metastasis Program, Ellen and Ronald Caplan Cancer Center of The Wistar Institute.**

This research revealed the importance of PAD4 protein in the migration of neutrophils, specialized white blood cells that serve as the first line of immune defense in the body, directly impacting both primary tumor growth and secondary malignant tumor spread. Both genetic deletion of PAD4 and pharmacological inhibition of PAD4 using Jubilant Therapeutic Inc's novel inhibitor dramatically down-regulated chemokine CXCR2, reduced immune suppressive polymorphonuclear myeloid derived suppressor cells (PMN-MDSCs) at tumor and metastatic sites, activated T cells, and synergized with immune checkpoint blockade.

All results point to a potent anti-tumor effect of PAD4 inhibition to target PMN-MDSCs in the tumor microenvironment. This finding is being further investigated in Wistar's Nefedova laboratory.

"These results highlight the potential of PAD4 inhibition as a novel treatment approach for cancer in addition to the previously established role of this pathway in autoimmune diseases," **said Luca Rastelli, Ph.D., Chief Scientific Officer, Jubilant Therapeutics Inc.** "We are developing several highly selective oral, small molecule PAD4 inhibitors, with the goal of bringing this novel mechanism to the clinic as potential therapeutics for tumor metastasis in colorectal and pancreatic cancers, patients with liver metastasis as well as for both acute and chronic autoimmune/inflammatory diseases."

These findings were only made possible through the supportive collaboration between Wistar, a Philadelphia based nonprofit biomedical research institute, and Jubilant Therapeutics Inc., a clinical-

stage precision therapy company developing new therapies to treat oncology and autoimmune disease.

"Only working together, we are able to efficiently translate our fundamental research discoveries into clinical realities," **states Heather Steinman, Ph.D., MBA, The Wistar Institute vice president for Business Development & executive director of Technology Transfer**.

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About:

The Wistar Institute is an international leader in biomedical research with special expertise in cancer research and vaccine development. Founded in 1892 as the first independent nonprofit biomedical research institute in the United States, Wistar has held the prestigious Cancer Center designation from the National Cancer Institute since 1972. The Institute works actively to ensure that research advances move from the laboratory to the clinic as quickly as possible. Wistar's Business Development Team is dedicated to advancing Wistar Science and Technology Development through creative partnerships. wistar.org.

Jubilant Therapeutics Inc. is a clinical stage precision therapeutics company advancing potent and selective small molecule modulators to address unmet medical needs in oncology and autoimmune diseases. Its advanced discovery engine integrates structure-based design and computational algorithms to discover and develop novel, precision therapeutics against both first-in-class and validated but intractable targets in genetically defined patient populations. The Company's advanced pipeline consists of a first in class dual epigenetic modifier, JBI-802, currently in a Phase I/II clinical trial to treat solid tumors, a novel brain-penetrant modulator of PRMT5 for which an IND has been accepted, a brain penetrant PDL1 inhibitor, as well as PAD4 inhibitors for oncology and inflammatory indications. The Company is headquartered in Bedminster, New Jersey and guided by globally renowned key opinion leaders and scientific advisory board members. For more: www.jubilanttx.com Twitter @JubilantTx, LinkedIn

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