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Aptose Announces Publication of Preclinical Data in AACR Journal Demonstrating Tuspentinib's Unique Mechanism of Action and Synthetic Lethality on AML Cells When Combined with Venetoclax

- *Peer-reviewed publication details unique TUS mechanism of action*
- *TUS+VEN combination synthetic lethality overcomes resistance to VEN*
- *Tuspentinib prolongs survival in multiple AML models resistant to other drugs*
- *Findings suggest TUS will demonstrate broad antileukemic activity across AML patients*
- *TUS+VEN+AZA Triplet Frontline Therapy in Newly Diagnosed AML Patients Now Enrolling*

SAN DIEGO and TORONTO, Dec. 12, 2024 (GLOBE NEWSWIRE) -- Aptose Biosciences Inc. ("Aptose" or the "Company") (NASDAQ: APTO, TSX: APS), a clinical-stage precision oncology company developing highly differentiated targeted agents to treat hematologic malignancies, today announced the publication of preclinical data for Aptose's lead hematology compound tuspentinib (TUS) in *Cancer Research Communications*, a journal of the American Association for Cancer Research (AACR), available online now [\(link\)](#).

The publication, entitled ***"Preclinical development of tuspentinib for the treatment of acute myeloid leukemia,"*** is the first preclinical profiling of tuspentinib, a well-tolerated, once daily, oral kinase inhibitor currently in clinical development for treatment of acute myeloid leukemia (AML). The publication defines TUS activities on select oncogenic signaling targets, demonstrates enhanced activity and safety of TUS when combined with other agents, and illustrates synthetic lethality when combined with venetoclax (VEN). Pharmacokinetic and toxicology studies revealed that TUS is readily absorbed and achieves plasma concentrations sufficient to inhibit the target kinases, it has a plasma half-life that supports once daily dosing, and it demonstrates a favorable safety profile.

Aptose is now enrolling newly diagnosed AML patients in a Phase 1/2 clinical study to receive the tuspentinib + venetoclax + azacitidine (TUS+VEN+AZA) triplet combination (NCT03850574). Clinical studies in patients with relapsed or refractory AML receiving TUS single agent or the TUS+VEN combination have been completed.

“The non-clinical findings presented in the publication suggest that TUS will demonstrate favorable safety and a breadth of antileukemic activity across AML patient populations with a diversity of adverse mutations, and the initial clinical data is bearing that out,” said William G. Rice, Chairman, President and Chief Executive Officer. “We are eager for the next set of data in our triplet combination trial of TUS+VEN+AZA.”

Key findings:

- Tuspentinib inhibits a defined cluster of oncogenic signaling kinases operative in AML
 - TUS inhibits SYK, JAK1/2, RSK2, mutant KIT, and wild type and mutant forms of FLT3
 - TUS potently killed AML lines (GI50 = 1.3 to 5.2 nM) and Ba/F3 cells expressing wildtype (GI50 = 9.1 nM) or various mutant forms of FLT3 (GI50 = 2.5 – 56 nM)
 - TUS dampens stroma-induced activation of FLT3-ITD signaling in AML cells
- TUS prolongs survival in multiple AML models
 - Oral TUS markedly extended survival in subcutaneously and orthotopically inoculated xenograft models of FLT3 mutant human AML, was well tolerated, and delivered enhanced activity when combined with venetoclax or 5-azacytidine
- TUS combines effectively with other classes of agents to kill AML cells with mutations in RAS and other difficult-to-treat adverse mutations
- TUS was 2.1-15-fold and a 4.5-13-fold more potent than gilteritinib at blocking fibrinogen and immunoglobulin-mediated activation of SYK in KG-1a cells
- The most notable observation was the marked and unexpected synthetic lethal vulnerability to venetoclax and two MCL1 inhibitors in the TUS-resistant cells

About Aptose

Aptose Biosciences is a clinical-stage biotechnology company committed to developing precision medicines addressing unmet medical needs in oncology, with an initial focus on hematology. The Company's small molecule cancer therapeutics pipeline includes products designed to provide single agent efficacy and to enhance the efficacy of other anti-cancer therapies and regimens without overlapping toxicities. The Company's lead clinical-stage, oral kinase inhibitor tuspentinib (TUS) has demonstrated activity as a monotherapy and in combination therapy in patients with relapsed or refractory acute myeloid leukemia (AML) and is being developed as a frontline triplet therapy in newly diagnosed AML. For more information, please visit www.aptose.com.

Forward Looking Statements

This press release may contain forward-looking statements within the meaning of Canadian and U.S. securities laws, including, but not limited to, statements relating to the therapeutic potential of tuspentinib, its clinical development and safety profile, including that it combines effectively with other classes of agents and will demonstrate a favorable safety profile and a breadth of antileukemic activity across an AML patient population with a diversity of adverse mutations, as well as statements relating to the Company's plans, objectives, expectations and intentions and other statements including words such as “continue”, “expect”, “intend”, “will”, “should”, “would”, “may”, and other similar expressions. Such statements reflect our current views with respect to future events and are subject to risks and uncertainties and are necessarily based upon a number of estimates and assumptions that, while considered reasonable by us are inherently subject to significant business, economic, competitive,

political and social uncertainties and contingencies. Many factors could cause our actual results, performance or achievements to be materially different from any future results, performance or achievements described in this press release. Such factors could include, among others: our ability to obtain the capital required for research and operations and to continue as a going concern; the inherent risks in early stage drug development including demonstrating efficacy; development time/cost and the regulatory approval process; the progress of our clinical trials; our ability to find and enter into agreements with potential partners; our ability to attract and retain key personnel; changing market conditions; inability of new manufacturers to produce acceptable batches of GMP in sufficient quantities; unexpected manufacturing defects; and other risks detailed from time-to-time in our ongoing quarterly filings, annual information forms, annual reports and annual filings with Canadian securities regulators and the United States Securities and Exchange Commission.

Should one or more of these risks or uncertainties materialize, or should the assumptions set out in the section entitled “Risk Factors” in our filings with Canadian securities regulators and the United States Securities and Exchange Commission underlying those forward-looking statements prove incorrect, actual results may vary materially from those described herein. These forward-looking statements are made as of the date of this press release and we do not intend, and do not assume any obligation, to update these forward-looking statements, except as required by law. We cannot assure you that such statements will prove to be accurate as actual results and future events could differ materially from those anticipated in such statements. Investors are cautioned that forward-looking statements are not guarantees of future performance and accordingly investors are cautioned not to put undue reliance on forward-looking statements due to the inherent uncertainty therein.

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