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# Aptose Announces Two Publications of Preclinical Data Elucidating the Anticancer Mechanism of Action of APTO-253

## ***Identification of APTO-253 target leading to inhibition of MYC expression in AML and hypersensitivity of cancer cells with BRCA1/2 deficiencies***

SAN DIEGO and TORONTO, June 04, 2018 (GLOBE NEWSWIRE) -- Aptose Biosciences Inc. (NASDAQ:APTO) (TSX:APS) today announced the publication of preclinical data elucidating the mechanism of action of APTO-253, the company's clinical stage anticancer product candidate. The data are published in two separate articles in the June 2018 issue (Volume 17, Number 6) of *Molecular Cancer Therapeutics*, a peer-reviewed journal of the American Association for Cancer Research (AACR).

The first publication, entitled "*APTO-253 stabilizes G-quadruplex DNA, inhibits MYC expression and induces DNA damage in acute myeloid leukemia cells,*" demonstrates that the APTO-253 small molecule anticancer agent inhibits expression of the MYC oncogene and depletes cells of the MYC protein, triggers the DNA repair and stress response pathways, and promotes programmed cell death (apoptosis) in acute myeloid leukemia (AML) cell lines and fresh bone marrow samples derived from patients with AML and other hematologic malignancies that often depend on MYC upregulation. The data demonstrate a multifaceted mechanism of action for APTO-253, primarily through engagement of select G-quadruplex DNA structures, one of which is located in the promoter of the MYC gene and is uniquely suited to targeting hematopoietic malignancies.

MYC dysregulation is a common driver in many malignancies, making it an attractive therapeutic target. Repression of MYC expression by bromodomain (BET) inhibitors has proven effective at triggering apoptosis in leukemia cells; however, inhibition of bromodomain proteins can cause severe toxicities and myelosuppression. Unlike BET inhibitors and other cancer chemotherapies, APTO-253 acts through a distinct mechanism and does not cause toxicity to normal bone marrow cells, as demonstrated across various species, including humans. And, as a first in class MYC inhibitor that does not cause myelosuppression, APTO-253 may be particularly appropriate for management of patients having AML and other hematologic malignancies with compromised bone marrow function.

The second publication, entitled "*APTO-253 is a new addition to the repertoire of drugs that can exploit DNA BRCA1/2 deficiency,*" expands on data from a poster presentation at the 2018 American Association for Cancer Research (AACR) Annual Meeting. This study identified a synthetic lethal interaction of APTO-253 in cancer cells deficient in BRCA1 or BRCA2 function, causing these cells to be hyper-sensitive to APTO-253. The research team found that APTO-253 stabilizes certain quadruplex DNA structures, which can elicit the DNA damage repair response and exhibit synthetic lethality comparable to olaparib – an FDA-

approved targeted therapy that acts against cancers in people with hereditary BRCA1 or BRCA1 mutations, including some ovarian, breast and prostate cancers, although through a different mechanism. The findings revealed for APTO-253 potential new solid tumor indications in which patients with defined mutations can be genetically identified.

“These data provide new insights into the mechanism of action of APTO-253 and add to our knowledge of how this novel agent inhibits expression of the MYC gene, an oncogene that promotes tumor growth and resistance to drugs in AML and other cancers,” said William G. Rice, Ph.D., Chairman, President and Chief Executive Officer.

### **About APTO-253**

APTO-253 is a clinical-stage small molecule targeted therapeutic agent that inhibits expression of the MYC oncogene, leading to cell cycle arrest and programmed cell death (apoptosis) in human-derived solid tumor and hematologic cancer cells, without causing general myelosuppression of the healthy bone marrow. The MYC oncogene is overexpressed in hematologic cancers, including acute myeloid leukemia (AML). Aptose researchers have reported the ability of APTO-253 to induce cell death, or apoptosis, in multiple blood cancer cell lines including AML, as well as *in vitro* synergy with various classes of conventional approved and investigational therapies for AML or myelodysplastic syndromes (MDS). New findings reveal that APTO-253 might also serve certain solid tumor patients with BRCA1/2 mutations, but without causing toxicity to the normal bone marrow functions.

### **About Aptose**

Aptose Biosciences is a clinical-stage biotechnology company committed to developing personalized therapies addressing unmet medical needs in oncology. Aptose is advancing new therapeutics focused on novel cellular targets on the leading edge of cancer. 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. For further information, please visit [www.aptose.com](http://www.aptose.com).

### **Forward Looking Statements**

This press release contains forward-looking statements within the meaning of Canadian and U.S. securities laws, including, but not limited to, statements regarding the clinical potential and favorable properties of APTO-253, potential combination drug studies, the re-initiation of its clinical trial and 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”, “potential” 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; 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 and economic 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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