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# Aptose Presents New Preclinical Data on CG-806 PAN-FLT3/PAN-BTK Inhibitor at ASH 60th Annual Meeting

## Data elucidate unique ability of CG-806 to overcome resistance to other FLT3 inhibitors in AML cells

SAN DIEGO and TORONTO, Dec. 03, 2018 (GLOBE NEWSWIRE) -- Aptose Biosciences Inc. (NASDAQ: APTO, TSX: APS) today announced the presentation of preclinical data from research led by The University of Texas MD Anderson Cancer Center exploring the mechanism by which CG-806, a highly potent pan-FLT3/pan-BTK inhibitor, overcomes the emergence of resistance common to other FLT3 inhibitors (FLT3i). The data were highlighted in a poster presentation on Sunday, December 2, 2018 at the American Society of Hematology (ASH) 60<sup>th</sup> Annual Meeting & Exposition, being held December 1-4 in San Diego, CA. Separately, Aptose and Oregon Health & Science University researchers also presented new data on CG-806 at ASH (see press release [here](#)).

The poster [Concomitant Targeting of FLT3 and BTK with CG-806 overcomes FLT3-Inhibitor Resistance Through Inhibition of Autophagy](#) discusses the importance of FLT3 targeted therapy for acute myeloid leukemia (AML), during which clinical benefit is often transient to current FLT3i and followed by FLT3i-resistance and treatment failure. In this study, all tested FLT3i-resistant cell lines bearing TKD or ITD+TKD mutations showed increased basal autophagy, phospho-BTK and phospho-FLT3 levels. CG'806, but not the FLT3 inhibitor quizartinib, reduced *in vitro* autophagy, phospho-BTK and phospho-FLT3 levels and efficiently killed FLT3-mutated cells, even in the presence of mesenchymal stem cells. Likewise, CG'806 exerted profound pro-apoptotic effects on primary AML patient cells harboring ITD+D835 mutations *ex vivo*. In a PDX model engrafted with the ITD+D835 mutated primary cells from a FLT3i-resistant AML patient, CG'806 significantly reduced leukemia cell burden and benefited mouse survival. The authors conclude the pan-FLT3/pan-BTK kinase inhibitor CG-806 may overcome FLT3i-resistance in AML through the simultaneous inhibition of FLT3, BTK and autophagy signaling, and that CG-806 represents an agent that may prevent or overcome FLT3 inhibitor resistance in AML patients.

Data were presented by members of the research team led by Michael Andreeff, M.D., Ph.D., Professor of Medicine, Haas Chair in Genetics, Department of Leukemia, at The University of Texas MD Anderson Cancer Center.

"Our mechanistic understanding of CG-806 continues to expand and distinguish the molecule from other FLT3 inhibitors," said William G. Rice, Ph.D., Chairman and Chief Executive Officer of Aptose. "As a pan-FLT3/pan-BTK multi-kinase inhibitor, CG-806 has the ability to overcome the rescue pathways that can lead to the acquired resistance seen with some current standard-of-care therapies. In addition, CG-806 has demonstrated a robust

safety profile in IND-enabling studies to date, and we look forward to advancing it to the clinic.”

### **About CG-806**

CG-806 is a preclinical stage oral, first-in-class pan-FLT3/pan-BTK multi-cluster kinase inhibitor. This small molecule demonstrates potent inhibition of wild type and all mutant forms of FLT3 (including internal tandem duplication, or ITD, and mutations of the receptor tyrosine kinase domain and gatekeeper region), eliminates acute myeloid leukemia (AML) tumors in the absence of toxicity in murine xenograft models, and represents a potential best-in-class therapeutic for patients with AML. Likewise, CG-806 demonstrates potent, non-covalent inhibition of the wild type and Cys481Ser mutant forms of the BTK enzyme, as well as other oncogenic kinase pathways operative in B cell malignancies, suggesting CG-806 may be developed for various B cell malignancy patients (including CLL, MCL, DLBCL and others) that are resistant/refractory/intolerant to covalent BTK inhibitors. It is in development for acute myeloid leukemia (AML) and B cell lymphoma.

### **About Aptose**

Aptose Biosciences is a clinical-stage biotechnology company committed to developing personalized therapies 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. APTO-253, the only clinical stage agent that directly targets the MYC oncogene and inhibits its expression, is in a Phase 1b clinical trial for the treatment of patients with relapsed or refractory acute myeloid leukemia (AML) or high risk MDS. CG-806 is an oral, first-in-class pan-FLT3/pan-BTK multi-cluster kinase inhibitor being developed to treat AML and certain B cell malignancies. 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 our intentions or current expectations concerning, among other things, the anti-tumor activity of CG-806, the clinical potential and favorable properties of CG-806, the IND filing and clinical trials for CG-806 and their expected timing, 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”, 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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