

## **Aptose Presents New Preclinical Data on CG'806 pan-FLT3/pan-BTK Inhibitor at ASH 59th Annual Meeting**

**Data elucidate unique ability of CG'806 to kill a broad range of AML cells by suppressing multiple pathways, to overcome resistance caused by bone marrow stromal cells, and to act synergistically with other agents**

SAN DIEGO and TORONTO, Dec. 11, 2017 (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 demonstrating that CG'806, a highly potent pan-FLT3/pan-BTK inhibitor, exerts a profound anti-leukemia effect in human and murine leukemia cell lines harboring FLT-3 ITD mutations, mutations that are usually associated with very poor prognoses in leukemia patients. In addition, CG'806 demonstrates apoptosis, or programmed cell death, in AML patient samples by several mechanisms and is able to overcome resistance that is seen with other FLT3 inhibitors. The data were highlighted in poster presentations on Sunday and Monday, December 10 and 11, 2017 at the American Society of Hematology (ASH) 59<sup>th</sup> Annual Meeting & Exposition, being held December 9-12 in Atlanta, GA.

The poster [\*\*The Pan-FLT3/BTK Multi-Kinase Inhibitor CG'806 Induces AML Killing in FLT-Mutant and Wild Type Cells, and Exerts Synergistic Pro-Apoptotic Effects with Concomitant Targeting of Anti-Apoptotic Bcl-2 and/or Mcl-1\*\*](#) demonstrated pronounced anti-leukemia activity of CG'806 against a broad array of AML cells, including those with FLT3-wild type, FLT3 with single mutations, or with FLT3 harboring dual ITD plus D835 or ITD plus F691 mutations, and it demonstrated synergistic effects in combination with Bcl-2 or Mcl-1 inhibitors even in FLT3 mutated AML cells. CG'806 elicited its broad spectrum killing of AML cells through its ability to suppress the FLT3 pathway as well the BTK, AURK, AKT and ERK signaling pathways that are differentially operative in different AML cells. Notably, CG'806 maintained cytotoxic activity against AML cells in the presence of FLT3 ligand and bone marrow stromal cells, and CG'806 demonstrated dose-dependent *in vivo* antitumor activity in a circulating AML murine model.

The poster [\*\*CG'806, a Novel Pan-FLT3/BTK Multi-Kinase Inhibitor, Induces Cell Cycle Arrest, Apoptosis or Autophagy in AML Cells Depending on FLT3 Mutation Status\*\*](#) further elucidated the anti-leukemia effect of CG'806. CG'806 exerted profound suppression of cell proliferation through G1 cell cycle arrest and induction of apoptosis in FLT3-mutant AML cells, which is associated with inhibition of mutant FLT3 signaling and the downstream p-AKT/p-mTOR/cyclin D1/p-Rb signaling axis. In contrast, CG'806 exerted a G2/M arrest in FLT3-wildtype (WT) cells through inhibition of aurora (AURK) and BTK kinases and induction of non-apoptotic cell death (autophagy or polyploidy). CG'806 sensitized AML cells

to standard chemotherapeutic agents cytarabine and idarubicin and significantly enhanced pro-apoptotic effects. Taken together, these data support the development of CG'806 for a diverse set of AML patients with FLT3-ITD, FLT3-ITD plus additional TKD/gatekeeper mutations, as well as FLT3-WT.

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.

The poster presentations can be accessed on the Events & Presentations section of the Aptose website at the following [link](#).

"As our mechanistic understanding of CG'806 grows, we are beginning to construct a framework of how a single molecule can inhibit specific clusters of kinases and kill a heterogeneous group of AML cells without observed toxicity to normal cells," commented 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 kill a broad range of AML cells through inhibition of multiple oncogenic pathways that are differentially expressed in subgroups of cells. It appears to overcome the limitations of competitive FLT3 inhibitory agents, to enhance the AML cell killing effects of certain other chemotherapies, and to exhibit a robust therapeutic index. We look forward to initiating clinical trials of CG'806 in 2018."

Separately, Aptose and Oregon Health & Science University Knight Cancer Center researchers also announced new data on CG'806 presented at ASH (see press release [here](#)).

In addition to the abstracts that were presented at ASH, two additional abstracts on CG'806 and two abstracts on APTO-253, Aptose's small molecule c-Myc Inhibitor, have been published on the [ASH abstracts site](#). All abstracts will become part of the permanent ASH and *Blood* abstracts archive.

### **About CG'806**

CG'806 is an oral, first-in-class pan-FLT3/pan-BTK inhibitor. This small molecule demonstrates potent inhibition of all wild type and mutant forms of FLT3 tested (including internal tandem duplication, or ITD, and mutations of the receptor tyrosine kinase domain and gatekeeper region), eliminates AML tumors in the absence of toxicity in murine xenograft models, and represents a potential best-in-class therapeutic for patients with FLT3-driven 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 kinases operative in B cell malignancies, suggesting CG'806 may be developed for CLL and MCL patients that are resistant/refractory/intolerant to covalent BTK inhibitors.

### **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 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 CG'806 and its clinical development 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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