October 30, 2023

Aptose Presents Highlights from Clinical Update Webcast Featuring Latest Available Data on AML Drug Tuspetinib

- *Tuspetinib (TUS) Combination with Venetoclax (VEN) Clinical Findings Highlighted*
- *TUS Targets VEN Resistance Mechanisms to Re-sensitize VEN Failure Patients to VEN*
- *44% ORR with TUS/VEN in Difficult-to-Treat VEN Failure R/R AML Patients*
- *48% ORR with TUS/VEN in Heavily Pre-treated R/R AML Patients*
- *Consistent Favorable Safety with TUS Single Agent and TUS/VENDoublet*

SAN DIEGO and TORONTO, Oct. 30, 2023 (GLOBE NEWSWIRE) -- Aptose Biosciences Inc. (“Aptose” or the “Company”) (NASDAQ: APTO, TSX: APS), a clinical-stage precision oncology company developing highly differentiated oral kinase inhibitors to treat hematologic malignancies, released highlights from a clinical update event held today, October 30, 2023, in conjunction with the European School of Haematology (ESH) 6th International Conference: Acute Myeloid Leukemia “Molecular and Translational”: Advances in Biology and Treatment, being held in Estoril, Portugal (the “ESH 2023 Conference”).

The webcast event featured a comprehensive review of up-to-date clinical data for Aptose’s lead compound tuspetinib (TUS) by Rafael Bejar, MD, PhD, Aptose’s Chief Medical Officer, and featured Naval G. Daver, MD, Professor, Director Leukemia Research Alliance Program, Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX. Dr. Daver is the lead investigator on Aptose’s APTIVATE trial of tuspetinib and is recognized for significant achievements in the development of novel acute myeloid leukemia (AML) treatments, including several combination therapies.

Tuspetinib (TUS) is a once-daily, oral, precision targeted kinase inhibitor that suppresses select kinases that drive the proliferation of AML. These key kinase targets include the SYK, FLT3, JAK1/2, mutant forms of KIT, RSK2, and the TAK1-TAB1 kinases operative in AML, while other kinases are avoided to promote safety.

AML care has shifted toward venetoclax (VEN) containing combination regimens and a new population of difficult-to-treat VEN relapsed patients (“VEN failures”) is emerging. Tuspetinib’s safety, activity, mechanism of action, and convenient dosing make it ideal for combination therapy. Importantly, TUS directly targets VEN resistance mechanisms (suppresses mutated FLT3, mutated KIT, SYK and mutated JAK1/2 of the JAK/STAT pathway, RSK2 of the RAS/MAPK pathway, key oncogenic growth and proliferation signals, and MCL-1 expression). This means that TUS targets pathways and may lead to re-sensitizing VEN-resistant cells to VEN when given in combination. TUS/VEN may safely and successfully treat these VEN failures, as we already have observed clinically, and an accelerated approval path may be available for VEN failure relapsed or refractory (R/R) AML

patients treated with TUS/VEN.

“We are really pleased by our growing safety and efficacy data on tuspetinib in very difficult-to-treat AML patient populations,” said Dr. Bejar. “This includes activity in FLT3-unmutated patients, a population that accounts for more than 70% of AML and has few effective treatment options. Additionally, tuspetinib’s significant activity in patients who have failed venetoclax treatment – a rapidly-emerging population of particularly high unmet medical need – provides a clear development pathway for tuspetinib with the potential for accelerated approval.”

“The safety and efficacy data we’ve seen with the tuspetinib/venetoclax combination is very encouraging, suggesting that tuspetinib may effectively treat the large number of VEN failures we are seeing frequently in our clinics,” said Dr. Daver. “Data from the TUS/VEN doublet gives us confidence to move tuspetinib forward into a TUS/VEN/HMA triplet for the treatment of frontline newly-diagnosed AML patients. Tuspetinib is an exciting agent, and I am happy to be part of the clinical development team.”

Clinical Findings

Aptose provided updated clinical findings from the ongoing APTIVATE study of tuspetinib:

Patient Enrollment

- More than 140 patients have been treated with tuspetinib to date
- 91 patients have received TUS as a single agent
- Aptose anticipated dosing up to 30 patients with TUS/VEN by the ESH 2023 Conference; however, investigator enthusiasm resulted in dosing of 49 patients (as of October 23, 2023), and patients continue being enrolled

Safety Profile

In the most recent data cut (October 23, 2023), the favorable safety profile remained consistent for TUS and TUS/VEN treated R/R AML patients:

- No TUS related adverse events (AEs) of QTc prolongation
- No observed differentiation syndrome
- No TUS related non-hematologic serious AEs
- No TUS related deaths
- No rhabdomyolysis or AEs of elevated creatine phosphokinase (CPK)
- No TUS related dose-limiting toxicities (DLT) from 20 mg level through 160 mg level
- One DLT of muscle weakness at 200 mg
    - Occurred in patient with high exposure
    - Not rhabdomyolysis │ No muscle destruction
- Avoids many typical toxicities observed with other FLT3, IDH1/2, and menin inhibitors
- In TUS/VEN doublet, no unexpected or new safety signals were observed

Tuspetinib Single Agent

- Tuspetinib as a single agent was well-tolerated and highly active among relapsed or refractory (R/R) AML patients with a diversity of adverse genotypes. TUS single agent delivered 42% and 60% CR/CRh response rates across all patients and across FLT3-

mutated patients, respectively, among evaluable VEN-naïve patients at the 80mg daily recommended phase 2 dose (RP2D)
- Tuspetinib demonstrated a 29% CR/CRh rate in VEN-naïve FLT3 unmutated (wildtype) AML at 80 mg daily RP2D, unlocking the potential for TUS to treat the additional 70-75% of the AML population without FLT3-mutation not currently addressed by any approved tyrosine kinase inhibitors
- Responses were achieved across four dose levels
- Responses were shown to mature over time with sustained blood count recovery during continuous dosing
- Several responders were bridged to potentially lifesaving transplant (HSCT)
- Durability was observed when HSCT was unavailable
- Tuspetinib single agent response rates compare favorably to gilteritinib FLT3 inhibitor

TUS/VEN Doublet (TUS 80mg/VEN 400mg)

- Patients who have failed venetoclax treatment represent an increasing AML population in need of improved salvage therapies
    - Over 90% of recent U.S. patients enrolled in the APTIVATE trial were VEN failures
- VEN resistance involves mutations in multiple pathways to evade BCL-2 blockade
    - Tuspetinib directly targets pathways involved in VEN resistance
    - By shutting down these pathways, tuspetinib appears to re-sensitize prior-VEN failures to venetoclax (see poster presented at the ESH 2023 Conference here)

Overall Response Rates (ORR) with TUS/VEN Doublet (see Table below, includes recent preliminary responses)

- 31 evaluable patients showed an ORR 48% (15 of 31)
- 81% (25 of 31) of patients were VEN failures
- 44% ORR (11 of 25) in VEN failures
- 60% ORR (6 of 10) in FLT3-mutant
- 43% ORR (9 of 21) in FLT3-wildtype
- Most patients are very early in treatment, having initiated dosing in the past 2-6 weeks, and responses are expected to mature over time

Overall Response Rates

Patient Population	Aug 1, 2023 10 patients evaluable of 15 dosed	Sep 1, 2023 15 patients evaluable of 26 dosed	Oct 23, 2023 31 patients evaluable of 49 dosed
Prior-VEN Failures	**44% (4 of 9)**	**38% (5 of 13)**	**44% (11 of 25)**
FLT3-Mutant	67% (2 of 3)	67% (4 of 6)	60% (6 of 10)
FLT3-Wildtype	43% (3 of 7)	33% (3 of 9)	43% (9 of 21)
Overall	50% (5 of 10)	47% (7 of 15)	48% (15 of 31)
Response Types	1CR|3CRi|1CRp	1CR|6CRi	2CR|7CRi|6PR

Multiple Planned Value-creating Milestones Ahead

- TUS/VEN incremental data readout in R/R AML planned: ASH 2023
- TUS/VEN further data on duration of response in R/R AML planned: 1Q & 2Q2024

- TUS/VEN/HMA planned initiation of pilot triplet study in 1L AML: 1H2024
- Extension into HR-MDS and CMML planned: 4Q2023

The associated slides from the presentation are available on Aptose's websitehere. The webcast of the presentation will be archived here.

About Aptose

Aptose Biosciences is a clinical-stage biotechnology company 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 has two clinical-stage oral kinase inhibitors under development for hematologic malignancies: tuspetinib (HM43239), an oral, myeloid kinase inhibitor being studied as monotherapy and in combination therapy in the APTIVATE international Phase 1/2 expansion trial in patients with relapsed or refractory acute myeloid leukemia (AML); and luxeptinib (CG-806), an oral, dual lymphoid and myeloid kinase inhibitor in Phase 1 a/b stage development for the treatment of patients with relapsed or refractory hematologic malignancies. 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 tuspetinib, its clinical development and safety profile and potential for accelerated approval, the value creating milestones planned for tuspetinib, 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.

For further information, please contact:

Aptose Biosciences Inc.
Susan Pietropaolo
Investor Relations
201-923-2049
spietropaolo@aptose.com

LifeSci Advisors, LLC
Dan Ferry, Managing Director
617-430-7576
Daniel@LifeSciAdvisors.com

Source: Aptose Biosciences, Inc.