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Aptose Reports Early Data Demonstrating Tuspetinib Improves Standard of Care Treatment Across Diverse Populations of Newly Diagnosed AML in Phase 1/2 TUSCANY Trial

- *Addition of Tuspetinib (TUS) to Venetoclax (VEN) and Azacitidine (AZA) is being developed as safe and mutation agnostic frontline therapy for AML*
- *Addition of TUS to VEN+AZA improves response rates; 100% CR/CRh at 80 mg and 120 mg*
- *Addition of TUS to VEN+AZA improves MRD-negativity rates; 78% among responders*
- *100% CR/CRh in FLT3 wildtype AML, representing 70% of AML population*
- *100% CR/CRh and MRD-negativity rates in TP53, RAS and FLT3*-ITD *mutated AML*
- *Broad spectrum activity and excellent safety profile continue at 120 mg dose to date*

SAN DIEGO and TORONTO, Aug. 18, 2025 (GLOBE NEWSWIRE) -- Aptose Biosciences Inc. (“Aptose” or the “Company”) (OTC: APTOF, TSX: APS), a clinical-stage precision oncology company developing the tuspetinib (TUS)-based triple drug frontline therapy to treat patients with newly diagnosed AML, today provided a data update from the Phase 1/2 TUSCANY trial in newly diagnosed AML. The trial was initiated in December 2024, and the growing body of positive data includes the recently completed third cohort of 120 mg TUS in the TUS+VEN+AZA triplet therapy. Data to date from ten (10) patients across all three cohorts, 40 mg, 80 mg or 120 mg TUS dose in TUS+VEN+AZA, support the use of TUS with standard of care treatment across all AML populations, including those carrying mutations that are the most difficult to treat and those with mutated and unmutated (wildtype) FLT3 genes.

The TUS+VEN+AZA triplet is being developed as a safe and well-tolerated mutation agnostic frontline therapy to treat large, mutationally diverse populations of newly diagnosed AML patients who are ineligible to receive induction chemotherapy. At the 120 mg TUS dose level in combination with VEN+AZA, as with the prior reported 40 mg and 80 mg TUS dose cohorts, no significant safety concerns or dose limiting toxicities (DLTs) have been observed in the TUSCANY trial, including no prolonged myelosuppression in Cycle 1 of subjects in remission, no reports of drug-related QTc prolongation or differentiation syndrome (DS), and no treatment-related deaths. Nine out of ten dosed patients remain on study across all dose cohorts and enrollment is being advanced to the 160 mg TUS dose level following the Cohort Safety Review Committee (CSRC) meeting.

“We already have data from three different TUS dose levels in the TUSCANY trial, and the data continue to strengthen at higher doses of TUS and over time. We are building a strong

case for TUS+VEN+AZA as a triplet frontline therapy of choice to address a broad AML population, including subgroups with the most adverse of mutations," said William G. Rice, Ph.D., Chairman, President and Chief Executive Officer of Aptose.

Data highlights:

Comparison of CR/CRh[1] Response rates[2-5]:

	VEN+AZA[2]	TUS+VEN+AZA
All subjects	65%	90% (9/10)
NPM1-mutant	67%	100% (2/2)
FLT3-ITD	61%	100% (2/2)
TP53-mutant	52%	100% (2/2)

Comparison of MRD-negativity[6] rates among All Subjects and among CR/CRh Responders[3]:

	VEN+AZA[2,3]	TUS+VEN+AZA
Among All Subjects	23.4%	70% (7/10)
Among CR/CRh Responders	40.9%	78% (7/9)

Comparison of MRD-negativity rates among more difficult-to-treat Patient Subpopulations defined as Lower Benefit (*TP53*-mutated) and Intermediate Benefit (*FLT3*-ITD or *RAS*-mutated) relative to VEN+AZA[5]:

	VEN+AZA[3,5]	TUS+VEN+AZA
Intermediate Benefit	27.9%	100% (3/3)
Lower Benefit	14.5%	100% (2/2)

TUS+VEN+AZA - CR/CRh and **MRD-negativity rates** among Subjects with Adverse Mutations:

TP53, FLT3-ITD, RAS mutations:	Achieved CR/CRh and MRD-negativity
	100% (5/5)

"As illustrated in the data highlights, the addition of TUS to VEN+AZA appears to boost response rates and MRD-negativity while maintaining favorable safety and tolerability," said Rafael Bejar, M.D., Ph.D., Chief Medical Officer of Aptose, "and the 100% CR/CRh and 100% MRD-negativity rates among the five biallelic *TP53*-mutant, *FLT3*-ITD, and *RAS*-mutant AML cases are exciting to see, as this can correlate with longer overall survival. We have observed a trend towards achieving CRs more quickly at the higher dose levels, so we are keen to see the activity as we advance into the 160 mg TUS dose cohort."

Key messages:

- Addition of TUS to VEN+AZA demonstrates excellent CR/CRh rates
  - 100% CR/CRh among all subjects treated at 80 mg and 120 mg TUS dose levels
  - Appear to be achieving CR earlier with 120 mg TUS than with 40 mg or 80 mg
- Addition of TUS to VEN+AZA demonstrates excellent MRD-negativity rates

    - MRD-negativity in 7 of 9 (78%) already achieved in patients who responded to therapy
    - Expect patient survival to be extended with continued long-term treatment
- Excellent safety and well tolerated with no dose-limiting toxicities (No DLT) at completed dose levels
- Broad-spectrum activity including patients with adverse *TP53*, *RAS* and *FLT3*-ITD mutations
- No loss of MRD-negativity observed to date, including in one patient with over 7 months of follow up
- MRD-negativity and remissions continue to mature over time on therapy
- No relapses reported to date and no treatment related deaths
- The only non-responder was a patient at the initial TUS dose level (40 mg) that did not achieve TUS exposures previously associated with response

Additional data are included in the new Aptose corporate presentationhere.

TUSCANY: TUS+VEN+AZA Triplet Phase 1/2 Study

The tuspetinib-based TUS+VEN+AZA triplet therapy is being advanced in the TUSCANY Phase 1/2 trial with the goal of creating an improved frontline therapy for newly diagnosed AML patients that is active across diverse AML populations, durable, and well tolerated.

The TUSCANY triplet Phase 1/2 study, being conducted at 10 leading U.S. clinical sites by elite clinical investigators, is designed to test various doses and schedules of TUS in combination with standard dosing of AZA and VEN for patients with AML who are ineligible to receive induction chemotherapy. A convenient, once daily oral agent, TUS is being administered in 28-day cycles. Multiple U.S. sites are enrolling in the TUSCANY trial with anticipated enrollment of 18-24 patients by late 2025. Data will be released as it becomes available.

More information on the TUSCANY Phase 1/2 study can be found on www.clinicaltrials.gov (here).

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 lead clinical-stage, oral kinase inhibitor tuspetinib (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 and safety profile of tuspetinib (including the triplet therapy) and its clinical development, the anticipated enrollment rate in the TUSCANY trial and the timing thereof, 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
Corporate Communications & Investor Relations
201-923-2049
spietropaolo@aptose.com

[1] Complete Response / Complete Response with Partial Hematological Recovery

[2] DiNardo et al. New England Journal of Medicine, August 2020; Volume 383(7):617-629.

[3] Pratz et al. Journal of Clinical Oncology, December 2021; Volume 40 (8):855-865.

[4] Othman et. al. Blood Neoplasia; September 2024; Volume 1 (3):1-11.

[5] Döhner et. al. Blood. 2024 November 21;144(21):2211-2222.

[6] MRD-negative indicates that the amount of Measurable Residual Disease, as assessed by central flow cytometry, is such that the proportion of leukemic cells in a bone marrow sample falls below <0.1%

Source: Aptose Biosciences, Inc.