

June 14, 2024



Aptose Presents Tuspentinib (TUS) Clinical and Preclinical Findings at European Hematology Association (EHA) 2024 Hybrid Congress

- *TUS Monotherapy and TUS+Venetoclax (VEN) Doublet Therapy Show Broad Clinical Activity and Strong Safety Data in relapsed or refractory (R/R) Acute Myeloid Leukemia (AML) and Differentiate TUS from other Investigational Drugs in AML*
- *TUS Monotherapy and TUS+VEN Doublet Therapy Active in Difficult-to-treat Genetic Subgroups, FLT3 Wildtype AML*
- *TUS Shown to Target VEN Resistance Mechanisms and Retain Activity on VEN-Resistant AML Cells in Preclinical Study*
- *TUS+VEN+Azacitidine (AZA) Triplet Trial to Treat Newly Diagnosed AML Patients; Clinical Sites Being Activated*

SAN DIEGO and TORONTO, June 14, 2024 (GLOBE NEWSWIRE) -- Aptose Biosciences Inc. ("Aptose" or the "Company") (NASDAQ: APTO, TSX: APS), a clinical-stage precision oncology company developing highly differentiated oral targeted agents to treat hematologic malignancies, today announced a clinical poster presentation and a preclinical e-poster at the European Hematology Association (EHA) 2024 Hybrid Congress in Madrid, Spain.

Tuspentinib (TUS) is being developed as a TUS + venetoclax (VEN) + hypomethylating agent (HMA) triple drug combination (or TUS+VEN+HMA triplet) as frontline therapy for newly diagnosed AML patients. Aptose's poster presentation illustrates the safety and breadth of activity of TUS monotherapy and the TUS+VEN doublet combination in relapsed or refractory (R/R) AML patients from the APTIVATE Phase 1/2 trial and supports the launch of the TUS+VEN+HMA (using azacitidine, AZA, as the HMA) triplet frontline therapy in newly diagnosed AML patients. Tuspentinib, a convenient once daily oral agent that potently targets SYK, FLT3, mutated KIT, JAK1/2, and RSK2 kinases, avoids many typical toxicity concerns observed with other agents. In the APTIVATE trial, TUS achieved broad activity across AML patients with a diversity of adverse genetics as a single agent and in combination with venetoclax in a very ill and heavily pre-treated AML population. Blast reductions and objective responses were observed in patients with prior-VEN, prior-FLT3 inhibitor (FLT3i) and prior-HSCT therapies, those with highly adverse genetics - including mutations in TP53 and RAS genes, and those with mutated or unmutated (wildtype) FLT3 genes.

"Our APTIVATE trial of tuspentinib as a monotherapy and in combination treatment with venetoclax in a very ill AML patient population, has yielded excellent, consistent safety and demonstrated clinical activity across a broad range of AML – including many with highly

adverse genetic mutations,” said Rafael Bejar, M.D., Ph.D., Corresponding Author and Chief Medical Officer of Aptose. “The AML treatment paradigm is quickly shifting to combination therapy for newly diagnosed AML patients, but current triplet therapies in development are limited by toxicities and are aimed at narrow subpopulations, leaving them unable to treat the larger AML population. Tuspentinib, with demonstrated broad activity and favorable safety/tolerability profile, appears to be an ideal third agent to add to a venetoclax and hypomethylating agent regimen. We and our clinical investigators are eager to initiate dosing of the TUS+VEN+AZA triplet study.”

TITLE: Safety and Efficacy of Tuspentinib as Monotherapy and Combined with Venetoclax in a Phase 1/2 Trial of Patients with Relapsed or Refractory (R/R) Acute Myeloid Leukemia (AML) (EHA ID # P557)

CONCLUSIONS

- **Extensive dose exploration** with **TUS** (93 patients) and **TUS+VEN** (79 patients) in **highly treatment experienced R/R AML patients** (prior VEN, FLT3i, HMA, chemotherapy, HSCT)
- **TUS monotherapy**
 - Complete remissions achieved at 40, 80, 120, and 160 mg with no DLT
 - 42% CRc and 50% ORR was observed in VEN naïve and FLT3-mutation harboring patients.
 - Responses achieved in patients harboring highly adverse genetics (TP53^{MUT}, RAS^{MUT}, other)
- **TUS+VEN Doublet**
 - Remains safe and well tolerated (40mg TUS + 400mg VEN | 80mg TUS + 400mg VEN)
 - Achieves bone marrow blast reductions and responses among diverse R/R AML patients with adverse mutations and prior failure of VEN
- **TUS targets known VEN resistance mechanisms *in vitro*** and is clinically active in both FLT3^{MUT} & FLT3^{WT} R/R AML populations even after prior VEN exposure.

AML 1L UNMET NEED AND TUS+VEN+HMA TRIPLET

Significant Unmet Medical Need in Frontline Newly Diagnosed AML

- Progress made with **VEN+HMA in 1L therapy** but 1/3 do not respond and median OS <15 months with <25% alive at 3-years.
 - Response rates and OS need improvement, especially in adverse genetic subgroups
 - Emergence of VEN resistance via RAS/MAPK, TP53, and FLT3 clonal expansion, among other mechanisms, compromises salvage therapies in R/R setting
- **A 3rd agent** is needed to boost responses with VEN+HMA standard of care therapy

TUS is Ideal 3rd Agent for Addition to VEN+AZA to Treat Newly Diagnosed AML

- TUS has **excellent safety** alone and in combination with **VEN** when co-administered
- TUS has **broad activity** across genetic subgroups including TP53, RAS/MAPK, &

FLT3 mutants

- TUS mechanism **may minimize drug resistance to VEN via inhibition of key AML kinases**
- TUS can be administered **with or without food** allowing co-administration with VEN
- Preliminary PK data suggest no clinically meaningful interaction between TUS and VEN requiring dose modification for co-administration.

In addition, a separate preclinical abstract was published as an e-poster publication at EHA:

TITLE: Tuspentinib Retains Nanomolar Potency Against AML Cells Engineered to Express the NRAS G12D Mutation or Selected for Resistance to Venetoclax (EHA ePoster ID # P1756).

The study demonstrated that TUS targets known venetoclax (VEN) resistance mechanisms, retaining nanomolar potency against AML cells engineered to express the NRAS-G12D mutation or selected for resistance to VEN, and in combination with VEN, could prevent emergence of resistance to both agents. TUS resistant cells showed hypersensitivity to VEN such that treatment with both drugs could also interfere with the emergence of TUS resistance.

To see the full poster presentations, please visit Aptose's website:

<https://www.aptose.com/investors/company-information/presentations>

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 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: tuspentinib (TUS), an oral, kinase inhibitor that 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; and luxepitinib (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 and safety profile of tuspentinib 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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