Aptose Announces Updated Clinical Responses, Breadth of Activity, and Safety Across Four Dose Levels of Tuspetinib in Difficult-to-Treat Acute Myeloid Leukemia Populations

- *Company Provides Comprehensive Clinical Update from Phase 1/2 Trial*
- *Tuspetinib Continues to Deliver Single Agent Responses in r/r AML Patients*
- *Tuspetinib Safety and Efficacy Profile may Position Drug to Become the Preferred Kinase Inhibitor for Triplet Combination, Maintenance Therapy, and Patients Failed by Prior FLT3 Inhibitors*
- *Tuspetinib Enrolling APTIVATE Expansion Trial for Monotherapy and Combination Therapy*
- *Luxeptinib Original Formulation Delivers New CR in DLBCL Patient*
- *Luxeptinib New G3 Formulation Continuous Dosing Ongoing in R/R AML Patients*
- *Aptose to Hold a Corporate Clinical Update and Data Review at 10:00 am EST*

SAN DIEGO and TORONTO and NEW ORLEANS, Dec. 11, 2022 -- Aptose Biosciences Inc. (“Aptose”) (NASDAQ: APTO, TSX: APS) today provided a clinical update of its lead oral myeloid kinome inhibitor, tuspetinib (formerly HM43239), as responses continue to emerge from a Phase 1/2 trial, and from its oral, dual lymphoid and myeloid kinase inhibitor, luxeptinib (formerly CG-806) in an ongoing Phase 1a/b trial.

Tuspetinib, a once daily oral agent designed to target FLT3, SYK, and JAK kinases but avoid targets that drive toxicities, safely delivered complete remissions (CR/CRh/CRi/CRp) as a monotherapy across four dose levels (40mg, 80mg, 120mg, and 160mg) in acute myeloid leukemia (AML) patients that previously had been failed by chemotherapy, Bcl-2 inhibitors, hypomethylating agents, competitor FLT3 inhibitors, and hematopoietic stem cell transplants. Data are being presented at the 2022 American Society of Hematology (ASH) annual meeting by lead investigator Naval G. Daver, M.D., Associate Professor in the Department of Leukemia at MD Anderson Cancer Center, showing tuspetinib delivers single agent responses in very ill and heavily pretreated relapsed or refractory AML patients of mutationally-defined populations, including those with AML harboring wild-type FLT3, ITD or TKD mutated FLT3, or mutated forms of NPM1, MLL,TP53, NRAS, KRAS, DNMT3A, RUNX1, various slicing factors, and other genes. “The welcome blend of safety and breadth of activity seen with tuspetinib in AML patients makes this an ideal candidate for combination therapy,” remarked Dr. Daver.

As of October 6, 2022, 60 heavily pretreated relapsed/refractory AML patients were enrolled at multiple centers and treated at doses escalating from 20 mg to 200 mg, with further dose exploration at the 40 mg, 80 mg, 120 mg and 160 mg dose levels. Prior to Aptose licensing tuspetinib, Hanmi Pharmaceutical Company demonstrated complete remissions at the 80 mg dose level. As of January 1, 2022, Aptose assumed control of clinical trial activities and has demonstrated additional complete remissions at the 120 mg, 160 mg, and now the 40 mg dose levels. Many responders were bridged successfully to hematopoietic stem cell transplant (HSCT), while others not eligible for HSCT remained on tuspetinib with a durable response and no drug related myelosuppression even after months of continuous dosing.

The noteworthy safety and potency profile position tuspetinib, in both FLT3 mutated (FLT3+) and wildtype (FLT3-WT) AML patients, potentially to become the kinase inhibitor of choice to combine with venetoclax and hypomethylating agents to deliver high response rates without exacerbated myelosuppression or life-threatening toxicities and potentially to become the preferred agent for maintenance therapy to prevent relapse after HSCT or drug-induced complete remissions. Such roles can define the ultimate therapeutic success for patients and commercial success for tuspetinib.

“While the superior target and safety profile, and proven breadth of activity of tuspetinib compared to competitive compounds in development advocate for tuspetinib to participate in broader and more sizable commercial markets,” said William G. Rice, Ph.D., Chairman, President, and Chief Executive Officer, “responses generated by tuspetinib in mutationally-defined populations of high unmet need may also provide accelerated approval opportunities.”

Highlights of Updated Tuspetinib Data

- In addition to 5 CRc and 1 PR reported at ASH 2021, 4 new CRc and 3 new PR have been generated thus far during 2022.
- New responses during 2022 were achieved with 160 mg,120 mg, 80 mg, and 40 mg
- Among efficacy evaluable patients treated with 80 mg, 120 mg, or 160mg, the following response rates were achieved:
    - FLT3+ 8 of 21 (38.1%)
    - FLT3-WT 4 of 21 (19%), plus additional CRi since data cutoff date
    - FLT3+ with prior FLT3i 3 of 11 (27.3%)

    - FLT3+/NPM1+ 4 of 6 (66.7%)
    - FLT3+/NPM1+/DNMT3A+ 3 of 4 (75%)
    - N/K-RAS+ 3 of 8 (37.5%)
- Significant bone marrow leukemic blast reductions were observed broadly in FLT3+ and FLT3 wildtype patients across multiple dose levels, comparable to reported gilteritinib data, but in more heavily pre-treated relapsed and refractory AML patients (waterfall chart available on Aptose website).
- Vignettes of patient experiences highlight the potency and breadth of tuspetinib to deliver complete remissions among several mutationally-defined populations with a diversity of adverse mutations.
- Tuspetinib continued to show a favorable safety profile with only mild AEs and no DLTs up to 160 mg per day, and no drug discontinuations from drug related toxicity.
    - No drug related SAE, drug related deaths, differentiation syndrome
    - No drug related AE of QT prolongation
    - No DLT through 160 mg level – one DLT of muscle weakness at 200 mg (not rhabdomyolysis)
    - No observed muscle destruction – no AE of elevated creatinine phosphokinase (CPK)
    - Avoids many of the typical toxicities observed with other tyrosine kinase inhibitors
- Aptose has identified a safe therapeutic range with a broad therapeutic window, spanning the dose levels of 40, 80, 120 and 160 milligrams.
- For the APTIVATE expansion trial that has initiated patient enrollment, Aptose has selected 120 mg as the initiating single agent expansion dose and 80 mg as the initiating dose selected for combination with venetoclax. The trial is designed to confirm activity through patient enrichment of specific mutationally defined AML populations, including FLT3 -mutant patients who have been failed by a prior FLT3 inhibitor, as supported by fast-track designation and a significant response rate to date.

More detail on the data is available on the presentations page of the Aptose website here.

Aptose also provided an update of the luxeptinib clinical program:

Luxeptinib Key Highlights

Luxeptinib is an oral, first-in-class FLT3 and BTK kinase inhibitor in Phase 1 a/b clinical studies for the treatment of myeloid hematologic malignancies. 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) and cures animals of AML in the absence of toxicity in murine leukemia models.

- Just recently, a CR was achieved with a diffuse large B-cell lymphoma (DLBCL) patient at the end of Cycle 22 with 900mg BID of the original G1 formulation. Previously, an MRD-negative CR was reported with a R/R AML patient receiving 450mg BID of the original G1 formulation. Collectively, these findings demonstrate luxeptinib is active against AML as well as lymphoid malignancies.
- The original G1 formulation of luxeptinib was hampered by poor absorption. The new “G3” formulation was designed and developed for more rapid absorption (early Tmax), more efficient absorption (use lower doses), longer retention (longer $t_{1/2}$), and greater accumulation (higher steady state levels).
- The new G3 formulation this year was tested as a single dose in 20 patients from a Phase 1 clinical program of luxeptinib. Modeling of the pharmacokinetic (PK) properties of G3 predicts steady-state plasma exposure from continuous dosing with 50 mg of G3 (every 12 hours, Q12h) should be comparable to that of 900 mg of the original G1 formulation Q12h, representing up to an 18-fold improvement in bioavailability with G3.
- Aptose recently announced dosing of the first patient with continuous dosing of the G3 formulation (50 mg BID) in an ongoing Phase 1a/b clinical trial in patients with relapsed or refractory AML. A second patient now has initiated continuous dosing with the G3 formulation.
- The G3 formulation may result in greater exposures of luxeptinib and additional responses in these difficult-to-treat patient populations.
- Aptose expects that 9-15 patients will determine if G3 is safe and achieves desired exposures to deliver clinical responses.

As announced prior, Aptose will be holding a conference call and data review today:

Aptose Corporate Update Details

Date & Time: Sunday, Dec 11, 2022, 10:00 AM EST

Participant Webcast Link: Link

Participant Dial-in:

Toll Free Investors Dial: 1-877-407-9039

Toll/International Investors Dial: 1-201-689-8470

Conference ID: 13734698

The slides will be available on Aptose’s website here and the webcast of the presentation will be archived shortly after the conclusion of the event at the link above.

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: tuspetinib (formerly HM43239), an oral, myeloid kinase inhibitor in an international Phase 1/2 trial in patients with relapsed or refractory acute myeloid leukemia (AML); and luxeptinib, 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 contains forward-looking statements within the meaning of Canadian and U.S. securities laws, including, but not limited to, statements regarding, the clinical development plans, the clinical potential, anti-cancer activity, therapeutic potential and applications and safety profile of tuspetinib and luxeptinib, the tuspetinib Phase 1/2 AML clinical trial, the luxeptinib Phase 1 a/b B-cell malignancy and Phase 1 a/b AML clinical trials and the upcoming milestones of such trials, the development and clinical potential of a new formulation (G3) for luxeptinib, upcoming updates regarding the clinical trials, and statements relating to the Company's plans, objectives, expectations and intentions and other statements including words such as "continue", "expect", "intend", "will", "hope" "should", "would", "may", "potential" 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; the potential impact of the COVID-19 pandemic and other risks detailed from time-to-time in our ongoing current reports, 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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