March 23, 2023

Aptose Reports Results for the Fourth Quarter and Full Year 2022

— APTIVATE Expansion Trial of Tuspetinib as Single Agent in Relapsed/Refractory AML Patients is Up and Running; Initiated Enrollment of Combination Treatment Arm with Venetoclax —

— RAS Mutated AML Clinically Sensitive to Tuspetinib —

— Continuous Dosing of G3 Formulation of Luxeptinib Ongoing —

— Conference Call and Webcast at 5:00 pm ET Today —

SAN DIEGO and TORONTO, March 23, 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, today announced financial results for the fourth quarter and year ended December 31, 2022, and provided a corporate update.

The net loss for the quarter ended December 31, 2022, was $10.0 million ($0.11 per share) compared with $24.3 million ($0.27 per share) for the quarter ended December 31, 2021. The net loss for the year ended December 31, 2022, was $41.8 million ($0.45 per share) compared with $65.4 million ($0.73 per share) for the year ended December 31, 2021. Total cash and cash equivalents and investments as of December 31, 2022, were $47.0 million. Based on current operations, Aptose expects that cash on hand and available capital provide the Company with sufficient resources to fund planned Company operations including research and development into the first quarter of 2024.

“To expand on the clinically significant response data observed across a broad population of acute myeloid leukemia (AML) patients during the dose escalation and exploration phase of our trial, we rapidly transitioned to our APTIVATE Phase 1/2 expansion trial with tuspetinib. APTIVATE already is running smoothly with several AML patients being treated in the monotherapy arm, and patient enrollment now is underway in the doublet combination treatment arm with tuspetinib and venetoclax (TUS/VEN). And we are eager to bring additional data to you throughout the year,” said William G. Rice, Ph.D., Chairman, President and Chief Executive Officer. “We anticipate enrolling up to 100 patients in the APTIVATE study, from which we expect to demonstrate single agent activity that can guide multiple paths for potential accelerated approval in patients with adverse mutations, and to demonstrate activity in doublet and then triplet combination therapies, which we believe represent the future directions of AML treatment. Tuspetinib’s single agent activity targets more AML populations than SYK inhibitors, IRAK4 inhibitors, or menin inhibitors, and, its distinctly favorable safety profile also lends itself to an ideal combination treatment to potentially treat larger AML patient populations in earlier lines of therapy.”

Key Corporate Highlights

- **Tuspetinib APTIVATE Expansion Trial Initiated** – In January, Aptose announced the initiation of dosing in the monotherapy arm in the APTIVATE Phase 1/2 clinical trial of tuspetinib (formerly HM43239), a once daily oral, mutation agnostic tyrosine kinase inhibitor being developed for the treatment of patients with relapsed or refractory acute myeloid leukemia (R/R AML). The APTIVATE expansion trial is designed to confirm monotherapy activity through patient enrichment of specific mutationally defined AML populations, including TP53-mutant patients and FLT3-mutant patients who have been failed by a prior FLT3 inhibitor, as supported by FDA fast-track designation and a clinically significant response rate to date. In the APTIVATE expansion trial, tuspetinib also will be tested in combination with venetoclax (TUS/VEN), and the TUS/VEN doublet arm already has begun enrollment. While APTIVATE is early in the treatment of patients with tuspetinib monotherapy, we already have observed initial signs of antileukemic activity, and we will provide additional color as the clinical data evolve.

  Tuspetinib is designed to simultaneously target SYK, JAK1/2, FLT3, RSK and other kinases operative in AML. As a monotherapy treatment during dose escalation and exploration in our Phase 1/2 trial, tuspetinib safely delivered multiple complete remissions and clinical responses across four dose levels (40mg, 80mg, 120mg, and 160mg) in AML patients that previously had been failed by chemotherapy, BCL2 inhibitors, hypomethylating agents, FLT3 inhibitors, and hematopoietic stem cell transplants. Data presented in December 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, showed tuspetinib delivers single agent responses without prolonged myelosuppression or life-threatening toxicities in these very ill and heavily pretreated R/R AML patients. Responses were observed in a broad range of mutationally-defined populations, including those with mutated forms of NPM1, MLL, TP53, DNMT3A, RUNX1, wild-type FLT3, ITD or TKD mutated FLT3, various splicing factors, and other genes. Unexpectedly, we observed a 29% CR/CRh response rate with tuspetinib monotherapy in patients having mutations in the RAS gene or other genes in the RAS pathway. Responses in RAS-mutated patients are important because the RAS pathway is often mutated in response to therapy by other agents as the AML cells mutate toward resistance to those other agents.

  With dose escalation and exploration successfully completed, we now are focusing on execution of the APTIVATE Phase 1/2 expansion trial. While we plan to report data throughout the year, we also will plan an incremental update from APTIVATE around the European Hematology Association (EHA) conference in June, a more complete dataset at the European School of Haematology (ESH) meeting in October, and even more data, including from the TUS/VEN combination cohort, during the ASH meeting in December.

- **Rationale for Tuspetinib's Superior Safety** –**-** Clinical responses by kinase inhibitors typically require high plasma exposures and near complete suppression of a target kinase, but such agents often cause undesired toxicities because they cause extensive inhibition of that same target in normal cells. In contrast, tuspetinib to date has demonstrated no drug related adverse events or dose-limiting toxicities over four active

dose levels, and Aptose recently elucidated a rationale for the superior safety profile of tuspetinib. Rather than causing near complete suppression of a single kinase, tuspetinib achieves clinical responses at lower plasma exposures by simultaneous fractional suppression of a small suite of kinases critical for leukemogenesis. This approach triggers apoptotic death of AML cells but does not result in extensive pathway suppression in normal cells that would lead to greater toxicities. Consequently, fractional suppression of a handful of key kinases and avoidance of safety-related kinases by tuspetinib circumvents many of the toxicities observed with competing agents.

- **Continuous Dosing of Luxeptinib "G3" Formulation Ongoing; Additional Luxeptinib Activity Noted** – In the fourth quarter of 2022, Aptose announced the initiation of dosing of the G3 formulation of luxeptinib, an oral, lymphoid and myeloid kinase inhibitor, in the ongoing Phase 1 a/b clinical trial in patients with R/R AML. G3 was developed for more rapid and efficient absorption of luxeptinib and it demonstrated a significant improvement in bioavailability, thereby enabling lower doses, longer retention and higher steady state levels of the drug. Initial pharmacokinetic (PK) data from continuous dosing of the 50 mg G3 formulation show plasma exposure levels roughly equivalent to the 900mg dose (18-fold greater dose) of the original G1 formulation. Aptose will be reviewing all data with the data monitoring committee and will make the determination to escalate and at what dose.

  Separately, a small number of B-cell patients are still receiving the original G1 formulation of luxeptinib at the 900 mg dose level. During ASH in December, we announced that a CR was achieved with a diffuse large B-cell lymphoma patient at the 900 mg dose level of the original G1 formulation, and we had previously reported an MRD-negative CR with a R/R AML patient receiving 450 mg BID of the original G1 formulation. Together, these findings demonstrate activity of luxeptinib in lymphoid malignancies and AML.

  Research on luxeptinib continues, and a non-clinical paper was published earlier this month in *PLOS One*, a highly respected online scientific publication. Titled, "Luxeptinib interferes with LYN-mediated activation of SYK and modulates BCR signaling in lymphoma," the paper helps to elucidate the mechanism by which Lux suppresses the B-cell receptor pathway in a manner distinct from the BTK inhibitor ibrutinib. Lux was more effective than ibrutinib at reducing both steady state and anti-IgM-induced phosphorylation of the LYN and SYK kinases upstream of BTK where ibrutinib has little or no effect, suggesting Lux can play a role in B-cell malignancies and inflammatory diseases distinct from ibrutinib and other BTK inhibitors.

- **Aptose Appoints VP, Controller** – During the fourth quarter, Aptose appointed Brooks Ensign, Vice President and Controller. Mr. Ensign has more than 20 years of pharmaceutical industry experience in accounting, finance and corporate development and has served in finance roles for multiple public and private companies, including Sunesis Pharmaceuticals, ISTA Pharmaceuticals and Amylin Pharmaceuticals. Mr. Ensign holds an M.B.A. from Harvard Business School and a Master's in Accounting from National University.

RESULTS OF OPERATIONS

A summary of the results of operations for the years ended December 31, 2022 and 2021 is presented below:

	Year ended December 31,	
(in thousands except per Common Share data)	2022	2021
Revenues	$ -	$ -
Research and development expenses	28,088	45,985
General and administrative expenses	14,514	19,462
Net finance income	779	93
Net loss	$ (41,823)	$ (65,354)
Unrealized gain/(loss) on securities available-for-sale	(2)	-
Total comprehensive loss	$ (41,825)	$ (65,354)
Basic and diluted loss per Common Share	$ (0.45)	$ (0.73)

Net loss of $41.8 million for the year ended December 31, 2022 decreased by approximately $23.5 million as compared with $65.4 million for the year ended December 31, 2021, primarily as of a result of a reduction in research and development program costs and personnel expenses of $5.4 million, the $12.5 million in license fees paid to Hanmi in 2021 for development rights of tuspetinib, and a $5.0 million decrease in general and administrative costs.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred related to the research and development of our product candidates. Costs include the following:

	Year ended December 31,	
(in thousands)	2022	2021
License fee – Tuspetinib	$ -	$ 12,500
Program costs – Tuspetinib	10,083	57
Program costs – Luxeptinib	8,426	18,490
Program costs – APTO-253	141	3,543
Personnel expenses	7,181	7,593
Stock-based compensation	2,218	3,790
Depreciation of equipment	39	12
Total	$ 28,088	$ 45,985

- External research and development expenses incurred under agreements with third parties, such as CROs, consultants, members of our scientific advisory boards, external labs and CMOs;

- Employee-related expenses, including salaries, benefits, travel, and stock-based compensation for personnel directly supporting our clinical trials and manufacturing, and development activities;

- License fees.

We have ongoing clinical trials for our product candidates tuspetinib and luxeptinib. Tuspetinib was licensed into Aptose in November 2021 and we assumed sponsorship, and the related costs, of the tuspetinib study effective January 1, 2022. In December 2021, we discontinued the APTO-253 program and are exploring strategic alternatives for this

compound.

We expect our research and development expenses to be higher as compared to 2022 for the foreseeable future as we continue to advance tuspetinib into larger clinical trials.

The research and development (“R&D”) expenses for the years ended December 31, 2022 and 2021 were as follows:

R&D expenses decreased by $17.9 million to $28.1 million for the year ended December 31, 2022 as compared with $46.0 million for the comparative period in 2021. Changes to the components of our R&D expenses presented in the table above are primarily as a result of the following activities:

- License fees paid in the year ended December 31, 2021 to Hanmi of $12.5 million for global development rights of tuspetinib, including $5.0 million in cash and $7.5 million in Common Shares. There were no license fee paid in the year ended December 31, 2022.

- Program costs for tuspetinib increased by $10.0 million. We in-licensed the development rights for tuspetinib in the fourth quarter of 2021 and assumed sponsorship, and the related costs, of the study effective January 1, 2022.

- Program costs for luxeptinib decreased by approximately $10.1 million, primarily due to lower manufacturing costs because the current formulation requires less API than the prior formulation, and lower clinical trial costs.

- Program costs for APTO-253 decreased by approximately $3.4 million due to the Company's decision on December 20, 2021 to discontinue further development of APTO-253.

- Personnel-related expenses decreased by $0.4 million, due to lower headcount in 2022.

- Stock-based compensation decreased by approximately $1.6 million in the year ended December 31, 2022, compared with the year ended December 31, 2021, primarily due to stock options granted with lower grant date fair values in the current period.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits and travel, including stock-based compensation for our executive, finance, business development, human resource, and support functions. Other general and administrative expenses and professional fees for auditing, and legal services, investor relations and other consultants, insurance and facility related expenses.

We expect that our general and administrative expenses will increase for the foreseeable future as we incur additional costs associated with being a publicly traded company and to support our expanding pipeline of activities. We also expect our intellectual property related legal expenses to increase as our intellectual property portfolio expands.

The general and administrative expenses for the years ended December 31, 2022 and 2021 are as follows:

	Year ended December 31,	
(in thousands)	2022	2021
General and administrative, excluding items below:	$ 11,444	$ 10,164
Stock-based compensation	2,989	9,160
Depreciation of equipment	81	138
Total	$ 14,514	$ 19,462

- General and administrative expenses for the year ended December 31, 2022 were approximately $14.5 million as compared with $19.5 million for the comparative period in 2021, a decrease of approximately $5.0 million. The decrease was primarily as a result of a decrease in stock-based compensation costs of $6.2 million, but was partially offset by higher salaries expenses, higher travel expenses, and higher professional fees.

- Stock-based compensation decreased by approximately $6.2 million mostly as a result of a lower number of options granted in the year ended December 31, 2022, with those options having a lower grant date fair value as compared with the options granted in the comparative period, and additional compensation recognized in the comparative period for modifications made to then vested and unvested stock options for one former company officer, as part of a separation and release agreement.

COVID-19 did not have a significant impact on our results of operations for the years ended December 31, 2022 and 2021. We have not experienced and do not foresee material delays to the enrollment of patients or timelines for the tuspetinib Phase 1/2 trial or the luxeptinib Phase 1a/b trials due to the variety of clinical sites that we have actively recruited for these trials. As of the date of this press release, we have not experienced material delays in the manufacturing of tuspetinib or luxeptinib related to COVID-19. Should our manufacturers be required to shut down their facilities due to COVID-19 for an extended period of time, our trials may be negatively impacted.

Conference Call & Webcast:

Date:	Thursday, March 23, 2023
Time:	5:00 PM ET
Audio Webcast Only:	link
Q&A Participant Registration Link*:	here

(https://register.vevent.com/register/BI9394078d0ea14714aca591ffe06992f1)

*Analysts interested in participating in the question-and-answer session will pre-register for the event from the participant registration link above to receive the dial-in numbers and a personal PIN, which are required to access the conference call. They also will have the option to take advantage of a Call Me button and the system will automatically dial out to connect to the Q&A session.

The audio webcast also can be accessed through a link on the Investor Relations section of Aptose's website here. A replay of the webcast will be available on the company's website for 30 days.

The press release, the financial statements and the management's discussion and analysis for the quarter and year ended December 31, 2022 will be available on SEDAR at www.sedar.com and EDGAR at www.sec.gov/edgar.shtml.

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 (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 contains forward-looking statements within the meaning of Canadian and U.S. securities laws, including, but not limited to, statements regarding the expected cash runway of the Company, the clinical development plans, the clinical potential, anti-cancer activity, therapeutic potential and applications and safety profile of tuspetinib and luxeptinib, the APTIVATE clinical trial, patient enrollment, potential accelerated approval, the luxeptinib Phase 1 a/b clinical trials and the upcoming milestones of such trials, the development and clinical potential of a new formulation (G3) for luxeptinib, expected variations in expenses, upcoming updates regarding the clinical trials, the exploration of strategic alternatives for the APTO-253 program, the expected impact of COVID-19 on results and operations 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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