

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**FORM 10-K**

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2022

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM  
TO

Commission File Number 001-3200

**Aptose Biosciences Inc.**

(Exact name of Registrant as specified in its Charter)

**Canada**

(State or other jurisdiction of  
incorporation or organization)

**251 Consumers Road, Suite 1105  
Toronto, Ontario, Canada M2J 4R3**

(Address of principal executive offices)

**98-1136802**

(I.R.S. Employer  
Identification No.)

**M2J 4R3**

(Zip Code)

Registrant's telephone number, including area code: **(647) 479-9828**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Shares, no par value	APTO	Nasdaq Capital Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes  No

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes  No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input type="checkbox"/>		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

The aggregate market value of the voting stock and nonvoting common equity held by non-affiliates computed by reference to the price at which the common equity was last sold, or the average bid and asked prices of such common equity, as of June 30, 2022 was \$68,270,348.

As of March 21, 2023, the registrant had 93,005,278 Common Shares outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

*Portions of our Proxy Statement for our 2023 Annual Meeting of Stockholders (the "Proxy Statement"), are incorporated by reference in Part III.*

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*This Annual Report on Form 10-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and is subject to the safe harbor created by those sections. For more information, see “Part I. Item 1. Business — Cautionary Note Regarding Forward-Looking Statements.”*

*As used in this report, the terms “Aptose,” “Aptose Biosciences,” the “Company,” “we,” “us,” “our” and similar references refer to Aptose Biosciences Inc. (formerly known as Lorus Therapeutics Inc.) and our consolidated subsidiaries, and the term “Common Shares” refers to our common shares, no par value.*

*Aptose had historically qualified as a “foreign private issuer” for purposes of reporting under the Exchange Act, and filing registration statements under the Securities Act of 1933, as amended. Effective December 31, 2018, however, Aptose ceased qualifying as a foreign private issuer and began filing reports with the United States Securities and Exchange Commission (“SEC”) as a “domestic issuer.” As a result, Aptose changed the accounting standards by which it prepares its financial statements from International Financial Reporting Standards to generally accepted accounting principles in the United States, or “U.S. GAAP.” All financial statements contained in this Annual Report are presented in accordance with U.S. GAAP. This report contains the following trademark, trade name and service mark of ours: Aptose. This report also contains trademarks, trade names and service marks that are owned by other persons or entities.*

## **PART I.**

### **ITEM 1. BUSINESS**

#### **Overview**

Aptose Biosciences Inc. (“Aptose,” the “Company,” “we,” “us,” or “our”) is a science-driven clinical-stage biotechnology company committed to precision medicines addressing the unmet clinical 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's executive offices are located in San Diego, California, and our head office is located in Toronto, Canada.

#### **Aptose Programs**

Aptose is advancing oral targeted agents to treat life-threatening cancers that, in most cases, are not elective for patients and require immediate treatment. We have two clinical-stage investigational products under active development for the treatment of hematologic malignancies: tuspentinib (HM43239), an oral, potent myeloid kinase inhibitor, and luxepetinib (CG-806), an oral, dual lymphoid and myeloid kinase inhibitor. Tuspentinib and luxepetinib are being evaluated for safety, tolerability, pharmacokinetics and signals of efficacy in Phase 1 clinical trials, while a third clinical asset not under active development is available for partnering (APTO-253). Each molecule is described below.

Tuspentinib is a once-daily oral potent myeloid kinase inhibitor, targeting a select group of kinases operative in myeloid malignancies and known to be involved in tumor proliferation, resistance to therapy, and differentiation but avoiding kinases that typically cause toxicities associated with other kinase inhibitors. Tuspentinib has completed the dose escalation and dose exploration stages of an international Phase 1/2 clinical trial designed to assess the safety, tolerability, pharmacokinetics, pharmacodynamic responses, and efficacy as a single agent in patients with relapsed or refractory (“R/R”) acute myeloid leukemia (“AML”). Complete responses (“CRs”) without dose limiting toxicities were achieved at four dose levels across a broad diversity of mutationally-defined AML populations and with a favorable safety profile. Moreover, tuspentinib to date has caused no QTc prolongations, liver or kidney toxicities, muscle damage or differentiation syndrome in treated patients and has caused no myelosuppression with continuous dosing of patients in remission. These findings led to the advancement of tuspentinib into the APTIVATE expansion trial of the Phase 1/2 program to collect responses in R/R AML patient populations enriched with specific genotypic backgrounds when treated with single agent tuspentinib or when combined with the venetoclax BCL-2 inhibitor, with the intent to guide selection of mutationally-defined AML populations for single agent Phase 2 Accelerated Approval Trial(s) and to position tuspentinib for dual and triple combination studies in later and early lines of therapy. Based on the safety and efficacy profile of tuspentinib, we believe that tuspentinib, if approved, can reach annual sales greater

than \$1 billion by 2035 because we believe tuspetinib could 1) become the preferred kinase inhibitor for inclusion in triplet combination for front line AML patients with FLT3 mutations and for patients with wild type FLT3, 2) become the preferred kinase inhibitor for inclusion in doublet combination with venetoclax for second line AML patients, 3) serve as an effective agent for maintenance therapy to prevent relapse in patients who achieved a complete remission through a stem cell transplant or through drug-based therapy, and 4) serve as an effective agent for the treatment of third line FLT3 mutated patients failed by prior therapy with other FLT3 inhibitors. However, our belief is based on management's current assumptions and estimates, which are subject to change, and there can be no assurance that tuspetinib will ever be approved or successfully commercialized and, if approved and commercialized, that it will ever generate significant revenues. See our "Risk Factors – "We are an early stage development company with no revenues from product sales." and "We have a history of operating losses. We expect to incur net losses and we may never achieve or maintain profitability." in this Annual Report on Form 10-K.

Luxepitinib is a novel, oral, highly potent lymphoid and myeloid kinase inhibitor that selectively targets defined clusters of kinases operative in myeloid and lymphoid hematologic malignancies. This small molecule anticancer agent has been evaluated in a Phase 1a/b study for the treatment of patients having B-cell leukemias and lymphomas that are resistant/refractory/intolerant to other therapies. Under a separate Investigational New Drug, Luxepitinib has been evaluated in a Phase 1a/b study for the treatment of patients with R/R AML or high risk MDS. These studies with the original formulation demonstrated tumor shrinkage among B-cell cancer patients, including a very recent report of a CR in a DLBCL patient that was determined via biopsy analysis at the end of Cycle 22 with 900mg BID dosing of the original G1 formulation. Likewise, a CR in one R/R AML patient occurred with 450mg BID dosing of the original G1 formulation. While these were important, absorption of the original G1 formulation hampered effectiveness of luxepitinib. To address the limited absorption of the G1 formulation, a new G3 formulation was developed and demonstrated improved absorption properties. The new G3 formulation is now being tested under conditions of twice daily continuous oral dosing in R/R AML patients. It is hoped the G3 formulation of luxepitinib can serve patients across lymphoid and myeloid malignancies and combine well with other agents to extend its application to multiple lines of therapy.

APTO-253 is a small molecule MYC oncogene inhibitor at the Phase 1a/b clinical trial stage of development for the treatment of patients with relapsed or refractory blood cancers, including AML and high-risk MDS. The clinical program was discontinued effective December 20, 2021, following a prioritization of the Company's other more advanced pipeline assets.

The following table sets the product candidates in our pipeline and their respective stages of development.

Pipeline Overview				
	Mechanism	Ownership	Preclinical	Clinical Stage Phase 1/2
<b>Tuspetinib*</b>	Myeloid Kinase	Aptose WW	AML	
<b>Luxeptinib**</b>	Lymphoid Kinase	Aptose: WW Crystal Genomics: Korea	CLL & NHL	
<b>Luxeptinib**</b>	Myeloid Kinase	Aptose: WW Crystal Genomics: Korea	AML & MDS	
<b>APTO-253</b>	MYC, KLF4	Aptose: WW	AML & MDS	
<b>APL-581</b>	BRD4/JAK	Aptose and Orm	Hematologic Cancers	

## Tuspetinib Program

### Inlicensing Overview

On November 4, 2021, we entered a licensing agreement with the South Korean company Hanmi Pharmaceutical Co Ltd. (“Hanmi”) for the clinical and commercial development of tuspetinib (formerly HM43239). Under the terms of the agreement, Hanmi granted Aptose exclusive worldwide rights to tuspetinib for all indications. Hanmi received an upfront payment of \$12.5 million, including \$5 million in cash and \$7.5 million in Common Shares. Hanmi will also receive up to \$407.5 million in future milestone payments contingent upon achieving certain clinical, regulatory and sales milestones across several potential indications, as well as tiered royalties on net sales. The term of the agreement will continue on a product-by-product and country-by-country basis until the expiration of the royalty period for such product in such country. The licenses to Aptose will survive and become non-exclusive, perpetual, irrevocable and fully paid-up on a product-by-product and country-by-country basis, upon their natural expiration under the terms of the agreement.

### Preclinical Profile

Tuspetinib is an oral, once-daily, highly potent myeloid kinase inhibitor designed to target key kinases operative in myeloid malignancies. In preclinical studies, tuspetinib demonstrated potent *in vitro* and *in vivo* activity against FLT3 ITD mutated as well as resistance-conferring D835 and gatekeeper (F691) tyrosine kinase domain (“TKD”) mutated AML. Additionally, tuspetinib inhibited phosphorylation of SYK, known to be highly activated in AML and associated with resistance to FLT3 targeted therapy. Tuspetinib also demonstrated inhibitory activity against several kinases involved in tumor cell proliferation and/or differentiation, including mutant forms of c-KIT, JAK1, JAK2, and RSK, with IC50 values < 10 nM.

Tuspetinib induced *in vitro* cytotoxicity in AML and Ba/F3 cell lines expressing FLT3 WT, ITD, and/or TKD point mutations. Tuspetinib showed greater inhibitory activity compared to quizartinib on Ba/F3 cells expressing resistance-conferring ITD/TKD double mutations (ITD/F691L and ITD/D835Y). Thus, Tuspetinib may overcome clinically relevant ITD/TKD double mutations, which may result from sustained FLT3 inhibition. Moreover, target modulation was shown as tuspetinib inhibited FLT3 phosphorylation and downstream signaling molecules such as phospho-ERK and phospho-STAT5.

The *in vivo* anti-tumor efficacy of tuspetinib was demonstrated in murine xenograft models using MV-4-11 and MOLM-13 human AML cells having the ITD mutant form of FLT3 and using the MOLM-14 model having the ITD and F691L dual mutations of FLT3 with dosing regimens that match those currently under investigation. Tuspetinib exhibited dose-dependent tumor growth inhibition of models of FLT3 ITD mutant AML with complete tumor regression observed in some groups, and no change in body weight. Of note, tuspetinib produced greater tumor growth inhibition in the MOLM-14 FLT3-ITD/F691L model compared to gilteritinib, or entospletinib (SYK inhibitor) as single agents, and comparable activity to the gilteritinib plus entospletinib combination.

#### *Latest Clinical Update and Program Status*

Tuspetinib has completed the dose escalation and dose exploration phases of an international Phase 1/2 study in patients with relapsed or refractory AML across clinical centers in the United States and South Korea. Clinical data from tuspetinib in AML were presented at the American Society of Hematology (ASH) Annual Meeting in December 2022 and presented during a Corporate Comprehensive Clinical Update Call held December 11, 2022. Data presented demonstrated that tuspetinib delivers single agent responses without prolonged myelosuppression or life-threatening toxicities in these very ill and heavily pretreated relapsed or refractory AML patients. Responses were observed in a broad range of mutationally-defined populations, including those with mutated forms of NPM1, MLL, TP53, NRAS, KRAS, DNMT3A, RUNX1, wild-type FLT3, ITD or TKD mutated FLT3, various splicing factors, and other genes. As of October 6, 2022, 60 heavily pretreated R/R 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. Tuspetinib delivered multiple CRs at 40 mg, 80 mg, 120 mg and 160 mg dose levels in which no dose limiting toxicities ("DLT") were observed. Tuspetinib demonstrated clinically meaningful benefit in all responders, by either bridging successfully to hematopoietic stem cell transplant (HSCT) or leading to a durable response, as well as a favorable safety profile. In addition to 5 CRc and 1 PR reported at ASH 2021, 4 new CRc and 3 new PR had been generated 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, response rates ranging from 19% to 75% were achieved in specific genotypic subpopulations of R/R AML patients. Significant bone marrow leukemic blast reductions were observed broadly in FLT3+ and FLT3 wildtype patients across multiple dose levels, comparable to reported gilteritinib data, except that the patients treated with tuspetinib were more heavily pre-treated relapsed and refractory AML patients than those treated with gilteritinib. 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, AE of QT prolongation or DLT were observed through the 160 mg level. Tuspetinib avoids many of the typical toxicities observed with other tyrosine kinase inhibitors. Aptose identified a safe therapeutic range with a broad therapeutic window, spanning the dose levels of 40, 80, 120 and 160 milligrams. Aptose also announced that enrollment had been initiated in the APTIVATE expansion trial for monotherapy and drug combination therapy with tuspetinib. For the APTIVATE expansion trial, Aptose selected 120 mg as the initiating single agent expansion dose and 80 mg as the initiating dose selected for combination with venetoclax.

As of January 30, 2023, Aptose announced the dosing of patients in the APTIVATE Phase 1/2 clinical trial of tuspetinib, and that another clinical response has been achieved by a R/R AML patient receiving 40 mg tuspetinib once daily orally in the original dose exploration trial, the second response at the recently launched low-dose 40 mg cohort. In addition, Aptose elucidated a rationale for the superior safety profile of tuspetinib. While several kinase inhibitors require high exposures that exert near complete suppression of a single target to elicit responses, those agents often cause additional toxicity because they also cause extensive inhibition of that target in normal cells. In contrast, tuspetinib simultaneously suppresses a small suite of kinase-driven pathways critical for leukemogenesis. Consequently, tuspetinib achieves clinical responses at lower exposures with less overall suppression of each pathway, thereby avoiding many toxicities observed with competing agents.

## **Luxepitinib Program**

### *Inlicensing Overview*

On May 7, 2018, we exercised an option by paying \$2.0 million in cash to the South Korean company Crystal Genomics, Inc. (“CG”) to purchase an exclusive license to research, develop and commercialize luxepitinib in all countries of the world except the Republic of Korea and China, for all fields of use (collectively, the “Rights”). Subsequently, on June 14, 2018, we announced that we entered into a license agreement with CG for Aptose to gain a license for rights to CG-806 in China (including the People’s Republic of China, Hong Kong, and Macau ) (the “China Rights”). Under the license agreement, Aptose made an upfront payment to CG of \$3.0 million for the China rights. CG is eligible for development, regulatory and commercial-based milestones, as well as single-digit royalties on product sales in China. The total deal value for the China Rights, including the upfront payment, is up to \$125 million. Aptose now owns worldwide (excluding Korea) rights to luxepitinib, a first-in-class, highly potent oral small molecule being developed for AML, B-cell malignancies, and other hematologic malignancies. Future possible royalties that might be paid under these agreements are determined on a country-by-country and product-by-product basis, on net sales during the period of time beginning on the first commercial sale of such product in such country and continuing until the later of: (i) the expiration of the last-to-expire valid claim of the CG Patents in such country covering such product; and (ii) ten (10) years after the first commercial sale of such product in such country.

### *Preclinical Profile*

Luxepitinib exhibits a picomolar half maximal inhibitory concentration (“IC50”) toward FLT3 with the Internal Tandem Duplication (“FLT3-ITD”), potency against the wild type FLT3 and a host of mutant forms of FLT3, as well as single-digit nanomolar IC50’s against BTK and its C481S mutant (“BTK-C481S”). Further, luxepitinib suppresses a small group of other relevant oncogenic kinases/pathways (including CSF1R, PDGFR $\alpha$ , TRK, and the ERK, MYC, AKT/mTOR/S6K and AURK/H3S10 pathways) that are operative in AML and certain B cell malignancies, but does not inhibit the TEC, epidermal growth factor receptor (EGFR) and ErbB2/4 kinases that are responsible for safety concerns with certain other kinase inhibitors.

As a potent inhibitor of FLT3-ITD, luxepitinib may become an effective therapy in a high-risk subset of AML patients. This is because the FLT3-ITD mutation occurs in approximately 30% of patients with AML and is associated with a poor prognosis. In murine xenograft studies of human AML (FLT3-ITD), CG-806 administered orally resulted in tumor elimination (“cures”) without measurable toxicity. Importantly, luxepitinib targets other oncogenic kinases which may also be operative in FLT3-ITD AML, thereby potentially allowing the agent to become an important therapeutic option for a broader group of this difficult-to-treat AML patient population. The findings that luxepitinib targets all forms of FLT3 and several other key oncogenic pathways, and that luxepitinib was well tolerated from a safety perspective during efficacy and formal Good Laboratory Practice (“GLP”) toxicology studies, suggest that luxepitinib may also have applicability in treating patients, particularly those over the age of 65, who cannot tolerate other therapies.

Separate from the AML and FLT3 story, luxetpinib may be a therapeutic option for patients with B cell malignancies. Overexpression of the BTK enzyme can drive oncogenic signaling of certain B cell malignancies, including CLL and certain NHL such as mantle cell lymphoma (“MCL”), follicular lymphoma (“FL”), diffuse large cell B cell lymphoma (“DLBCL”) and others. Therapy of these patients with covalent, irreversible BTK inhibitors, such as ibrutinib, that target the active site cysteine (“Cys”) residue of BTK can be beneficial in many patients. However, therapy with covalent BTK inhibitors can select for BTK with a C481S mutation, thereby conferring resistance to covalent BTK inhibitors. Furthermore, approximately half of CLL patients have discontinued treatment with ibrutinib after 3.4 years of therapy. Discontinuation of ibrutinib is due to the development of drug resistance (in particular, patients have malignancies that developed the BTK-C481S mutation), or due to refractory disease (patient tumors did not respond to ibrutinib) or intolerance (side effects led to discontinuation of ibrutinib), according to a study performed at The Ohio State University. The C481S mutation is observed in 5-10% of the patients, while 40-45% of the patients were intolerant or refractory to ibrutinib. As a non-covalent, reversible inhibitor of BTK, luxetpinib does not rely on the Cysteine 481 residue (“C481”) for inhibition of the BTK enzyme. Indeed, recent X-ray crystallographic studies (with wild type and C481S BTK) demonstrated that luxetpinib binds productively to the BTK active site in a manner that is indifferent to the presence or absence of mutations at the 481 residue. Moreover, *in vitro* studies demonstrated that luxetpinib kills B cell malignancy cell lines on average approximately 1000 times more potently than ibrutinib and kills ibrutinib-resistance cancer cells, and that luxetpinib more potently killed primary malignant cells taken from the bone marrow of CLL and ALL B-cell cancer patients. Yet, luxetpinib demonstrated a high degree of safety in animal efficacy and GLP toxicology studies. Consequently, patients who are resistant, refractory or intolerant to ibrutinib or other commercially approved or development-stage BTK inhibitors with B cell malignancies may continue to be sensitive to luxetpinib therapy. This is particularly true since luxetpinib inhibits the wild type and mutant forms of BTK, as well as other kinases/pathways that drive the survival and proliferation of B cell malignancies.

#### *Latest Clinical Update and Program Status*

Luxetpinib is currently being evaluated in a Phase 1 a/b trial in patients with relapsed or refractory B cell malignancies who have failed or are intolerant to standard therapies, and in a separate Phase 1 a/b trial in patients with relapsed or refractory AML or high-risk MDS. During 2022, a new G3 formulation was tested as a single dose in 20 patients during the ongoing Phase 1 a/b clinical program. Modeling of the pharmacokinetic (PK) properties of G3 predicted 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 a significant improvement in bioavailability with G3. On November 14, 2022, Aptose announced dosing of the first AML patient to receive a continuous dosing regimen of the G3 formulation (50 mg G3 Q12h), with the protocol allowing for further dose escalation of G3 in subsequent patients. Clinical data from both studies were presented during a Corporate Comprehensive Clinical Update Call held December 11, 2022. During the Corporate Update Call, Aptose announced 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. Aptose expects that dosing 9-15 patients will determine if G3 is safe and achieves desired exposures to deliver clinical responses.

#### **APTO-253 Program**

APTO-253 is a novel small molecule therapeutic agent that inhibits expression of the MYC oncogene, leading to cell cycle arrest and programmed cell death (apoptosis) in human-derived solid tumor and hematologic cancer cells, without causing general myelosuppression of the healthy bone marrow. MYC is a transcription factor that regulates cell growth, proliferation, differentiation and apoptosis, and overexpression amplifies new sets of genes to promote oncogenesis.

The clinical development of APTO-253 began in January 2011, with a Phase 1 dose-escalation study in patients with advanced or metastatic solid tumors. The clinical program of APTO-253 more recently also included a Phase 1a/b dose escalation study in patients with relapsed or refractory AML or high risk MDS, during which no objective responses were observed.



On December 20, 2021, Aptose announced the decision to discontinue further clinical development of APTO-253. The decision resulted from a strategic prioritization of the company's resources to focus on more advanced pipeline candidates, as well as an internal review of the product profile and performance to date of APTO-253, including a clinical hold placed by the U.S. Food & Drug Administration ("FDA").

### **Competitive Conditions**

The biotechnology and pharmaceutical industries are characterized by rapidly evolving technology and intense competition. There are numerous companies in these industries that are focusing their efforts on activities similar to ours. Some of these are companies with established positions in the pharmaceutical industry and may have substantially more financial and technical resources, more extensive research and development capabilities, and greater marketing, distribution, production, and human resources than Aptose. In addition, we face competition from other companies for opportunities to enter partnerships with biotechnology and pharmaceutical companies and academic institutions.

Competition with our potential products may include chemotherapeutic agents, monoclonal antibodies, antisense therapies, small molecules, immunotherapies, vaccines, and other biologics with novel mechanisms of action. These drugs may kill cancer cells indiscriminately, or through a targeted approach, and some have the potential to be used in non-cancer indications. We also expect that we will experience competition from established and emerging pharmaceutical and biotechnology companies that have other forms of treatment for the cancers that we target, including drugs currently in development for the treatment of cancer that employ a number of novel approaches for attacking these cancer targets. Cancer is a complex disease with more than 100 indications requiring drugs for treatment. The drugs in competition with our potential drugs have specific targets for attacking the disease, targets which are not necessarily the same as ours. These competitive drugs, however, could potentially also be used together in combination therapies with our drugs to manage the disease. Other factors that could render our potential products less competitive may include the stage of development, where competitors' products may achieve earlier commercialization, as well as superior patent protection, better safety profiles, or a preferred cost-benefit profile.

#### *Tuspetinib and Luxeptinib for AML*

We also face intense competition in AML as there is a wide range of therapies that have been approved and are under development for the treatment of AML. Companies that have developed approved therapies include Jazz (VYXEOS), Pfizer (MYLOTARG), Novartis (RYDAPT), Astellas (XOSPATA), Servier (TIBSOVO), Rigel (REZLIDHA), and AbbVie (VENCLEXTA), among others. Others are currently developing targeted therapies such as FLT3 inhibitors which include Daiichi Sankyo (quizartinib), Arog (crenolanib), IDH1/2 inhibitors which include Celgene/BMS (IDHIFA), SYK inhibitors which include Kronos Bio (lanraplenib), IRAK4 inhibitors which include Curis (emavusertib), and menin inhibitors which include Syndax (revumenib, SNDX-5613) and Kura (KO-539), among others.

#### *Luxeptinib for B Cell Malignancies*

We are aware of a number of companies that have developed and are pursuing different approaches to BTK inhibition, both for the wild type and to the C481S-mutant forms. Companies that have developed approved or are currently developing inhibitors that directly target the wild type include AbbVie (IMBRUVICA), AstraZeneca (CALQUENCE), and Beigene Co., Ltd. (Zanubrutinib). Others that are developing inhibitors that target the C481S-mutant BTK include Merck (nemtabrutinib), and Eli Lilly (pirtobrutinib), among others.

## **Manufacturers, Suppliers and Other Third-Party Contractors**

Contract manufacturing organizations (“CMOs”) manufacture our product candidates for all preclinical studies and clinical trials. We rely on CMOs for manufacturing, filling, packaging, storing and shipping of drug product in compliance with Current Good Manufacturing Practice (“cGMP”) regulations applicable to our products. The FDA ensures the quality of drug products by carefully monitoring drug manufacturers’ compliance with cGMP regulations. The cGMP regulations for drugs contain minimum requirements for the methods, facilities and controls used in manufacturing, processing and packing of a drug product. These CMOs are reputable companies active in the biotechnology industry. Pricing is predictable as there are many alternatives for such supplies that are readily available.

We rely and will continue to rely on third party contract research organizations (“CROs”) to conduct a significant portion of our preclinical and clinical development activities. Preclinical activities include *in vivo* studies providing access to specific disease models, pharmacology and toxicology studies, and assay development. Clinical development activities include trial design, regulatory submissions, clinical patient recruitment, clinical trial monitoring, clinical data management and analysis, safety monitoring and project management, contract manufacturing and quality assurance.

## **Intellectual Property**

We believe that our issued patents and pending applications are important in establishing and maintaining a competitive position with respect to our products and technology.

### *Tuspetinib (HM43239)*

In November 2021, we licensed the exclusive rights to research, develop and commercialize tuspetinib. Under the terms of the agreement, Hanmi has granted Aptose exclusive worldwide rights to tuspetinib for all indications. Aptose is now the exclusive licensee of composition of matter and use patents covering tuspetinib, and tuspetinib analogs. Aptose believes that it now owns rights to a strong and defensive intellectual property position.

As of December 31, 2022, Aptose owns rights in 39 issued patents, including 3 issued U.S. patents, and 22 patents validated in countries in Europe, that are in force and cover the tuspetinib compound, or analog compounds. These patents are expected to provide protection until 2038-2039. Patent applications are also pending in the United States and in contracting states to the Patent Cooperation Treaty for coverage of tuspetinib and analog compounds, with expected expiry dates between 2038-2042.

### *Luxeptinib (CG-806)*

In May 2018 and June 2018, we licensed the Rights to CG-806, for all fields of use, in all territories outside of the Republic of Korea and China, by exercising an option we obtained through a June 2016 option-license agreement with CG that had granted us an exclusive option to research, develop and commercialize CG-806. In June 2018, we entered into a separate license agreement with CG for Aptose to gain a license for the China Rights. Aptose now owns worldwide Rights to CG-806, including an issued patent in China but excluding any Rights in Korea.

As of December 31, 2022, Aptose owns rights to 46 issued patents, including 3 issued U.S. patents, and 30 patents validated in countries in Europe, that are in force and cover numerous compounds, including the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and methods of use for treating various diseases by administering various compounds, including the CG-806 compound. These patents are expected to provide protection until 2033-2038. Patent applications are also pending in the United States and in contracting states to the Patent Cooperation Treaty for coverage of CG-806, with expected expiry dates between 2038-2039.

### **Environmental Protection**

The Company's research and development activities involve the controlled use of hazardous and radioactive materials and, accordingly, the Company is subject to federal, provincial and local laws and regulations in the United States and Canada governing the use, manufacture, storage, handling and disposal of such materials and certain waste products. To the knowledge of the Company, compliance with such environmental laws and regulations does not and will not have any significant impact on its capital spending, profits or competitive position within the normal course of its operating activities. There can be no assurance, however, that the Company will not be required to incur significant costs to comply with environmental laws and regulations in the future or that its operations, business or assets will not be materially adversely affected by current or future environmental laws or regulations.

### **Employees**

As of December 31, 2022, we employed 35 full-time persons and one part-time person in research and drug development and administration activities. Eleven of our employees hold Ph.D.s, two hold M.D.s, and numerous others hold degrees and designations such as M.Sc., B.Sc., C.P.A., C.M.A., M.Acc. and M.B.A. To encourage a focus on achieving long-term performance, employees and members of the board of directors of the Company (the "Board") have the ability to acquire an ownership interest in the Company through Aptose's share option and alternate compensation plans.

The business of the Company requires personnel with specialized skills and knowledge in oncology. Researchers must be able to design and implement studies to assess the efficacy of anticancer drugs. Specialized knowledge and skills relating to chemistry and formulation process development are also needed. Such knowledge and skills are needed to develop product specific analytical methods and formulation processes. The Company's business also requires clinical and regulatory expertise and knowledge. The Company has trained scientists and personnel with broad experience in these fields.

None of our employees are unionized, and we consider our relations with our employees to be good.

### **Government Regulation**

#### *Overview*

Our overall regulatory strategy is to work with the appropriate government departments which regulate the use and sale of therapeutic drug products. This includes the FDA in the United States, Health Canada in Canada, the European Medicines Agency ("EMA") in Europe, and other local regulatory agencies with oversight of preclinical studies, clinical trials and marketing of therapeutic products. Where possible, we intend to take advantage of opportunities for accelerated development of drugs designed to treat rare and serious or life-threatening diseases. We also intend to pursue priority evaluation of any application for marketing approval filed in Canada, the United States or the European Union and to file additional drug applications in other markets where commercial opportunities exist. We may not be able to pursue these opportunities successfully.

Regulation(s) by government authorities in the United States, Canada, and the European Union are significant factors in guiding our current research and drug development activities. To clinically test, manufacture and market drug products for therapeutic use, we must be in compliance with guidance and regulations established by the regulatory agencies in the countries in which we currently operate or intend to operate.

The laws of most of these countries require the licensing of manufacturing facilities, carefully controlled research and the extensive testing of products. Biotechnology companies must establish the safety and efficacy of their new products in clinical trials; they must establish and comply with cGMPs for the manufacturing of the product and control over marketing activities before being allowed to market a product. The safety and efficacy of a new drug must be shown through human clinical trials of the drug carried out in accordance with the guidance and regulations established by local and federal regulatory agencies.

The process of completing clinical trials and obtaining regulatory approval for a new drug takes a number of years and requires the expenditure of substantial resources. Once a new drug or product license application is submitted, regulatory agencies may not review the application in a timely manner and may not approve the product. Even after a New Drug Application (“NDA”) submission has occurred and/or approval has been obtained, further studies, including post-marketing studies, may be required to provide additional data on the efficacy and safety necessary to confirm the approved indication or to gain approval for the use of the new drug as a treatment for clinical indications other than those for which the new drug was initially tested. Also, regulatory agencies require post-marketing surveillance programs to monitor a new drug’s side effects, safety and long-term effects of the product. A serious safety or effectiveness problem involving an approved new drug may result in a regulatory agency mandating a withdrawal of the new drug from the market and possible civil action. It is possible that we could encounter such difficulties or excessive costs in our efforts to secure necessary approvals, which could delay or prevent us from manufacturing or marketing our products.

In addition to the regulatory product approval framework, biotechnology companies, including Aptose, are subject to regulation under local, provincial, state and federal law, including requirements regarding occupational safety, laboratory practices, environmental protection and hazardous substance control, and may be subject to other present and future local, provincial, state, federal and foreign regulation, including possible future regulation of the biotechnology industry.

#### *Approval of New Drugs in Canada*

In Canada, the manufacture and sale of new drugs are controlled by Health Canada. New drugs must pass through a number of testing stages, including pre-clinical testing and human clinical trials. Pre-clinical testing involves testing the new drug’s chemistry, pharmacology and toxicology *in vitro* and *in vivo*. Successful results (that is, potentially valuable pharmacological activity combined with an acceptable low level of toxicity) enable the developer of the new drug to file a clinical trial application to begin clinical trials involving humans.

To study a drug in Canadian patients, a clinical trial application submission must be filed with Health Canada. The clinical trial application submission must contain specified information, including the results of the pre-clinical tests completed at the time of the submission and any available information regarding use of the drug in humans. In addition, since the method of manufacture may affect the efficacy and safety of a new drug, information on manufacturing methods and standards and the stability of the drug substance and dosage form must be presented. Production methods and quality control procedures must be in place to ensure an acceptably pure product, essentially free of contamination, and to ensure uniformity with respect to all quality aspects.

In addition, all federally regulated trials must be approved and monitored by an independent committee of doctors, scientists, advocates and others to ensure safety and ethical standards, Institutional Review Boards (“IRBs”) or Ethics Review Boards (“ERBs”). The review boards study and approve all study-related documents before a clinical trial begins and also carefully monitor data to detect benefit or harm, and validity of results.

Provided Health Canada does not reject a clinical trial application submission and IRB or ERB approval has been obtained, clinical trials can begin. Clinical trials for product candidates in Canada, as in the United States, are generally carried out in three phases. Phase 1 involves studies to evaluate toxicity and ideal dose levels in healthy humans. The new drug is administered to human patients who have met the clinical trial entry criteria to determine pharmacokinetics, human tolerance and prevalence of any adverse side effects. Phases 2 and 3 involve therapeutic studies. In Phase 2, efficacy, dosage, side effects and safety are established in a small number of patients who have the disease or disorder that the new drug is intended to treat. In Phase 3, there are controlled clinical trials in which the new drug is administered to a large number of patients who are likely to receive benefit from the new drug. In Phase 3, the effectiveness of the new drug in patients is compared to that of standard accepted methods of treatment in order to provide sufficient data for the statistical proof of safety and efficacy for the new drug.

If clinical studies establish that a new drug has value, the manufacturer submits a new drug submission application to Health Canada for marketing approval. The new drug submission contains all known information known about the new drug, including the results of pre-clinical testing and clinical trials. Information about a substance contained in new drug submission includes its proper name, its chemical name, and details on its method of manufacturing and purification, and its biological, pharmacological and toxicological properties. The new drug submission also provides information about the dosage form of the new drug, including a quantitative listing of all ingredients used in its formulation, its method of manufacture, manufacturing facility information, packaging and labeling, the results of stability tests, and its diagnostic or therapeutic claims and side effects, as well as details of the clinical trials to support the safety and efficacy of the new drug. Furthermore, for biological products, an on-site evaluation is completed to assess the production process and manufacturing facility. It is required prior to the issuance of a notice of compliance. All aspects of the new drug submission are critically reviewed by Health Canada. If a new drug submission is found satisfactory, a notice of compliance is issued permitting the new drug to be sold for the approved use. In Canada, an establishment license must be obtained prior to marketing the product.

Health Canada has a policy of priority evaluation of new drug submissions for all drugs intended for serious or life-threatening diseases for which no drug product has received regulatory approval in Canada and for which there is reasonable scientific evidence to indicate that the proposed new drug is safe and may provide effective treatment.

An exception to the foregoing requirements relating to the manufacture and sale of a new drug is the limited authorization that may be available in respect of the sale of new drugs for emergency treatment. Under the special access program, Health Canada may authorize the sale of a quantity of a new drug for human use to a specific practitioner for the emergency treatment of a patient under the practitioner's care. Prior to authorization, the practitioner must supply Health Canada with information concerning the medical emergency for which the new drug is required, such data as is in the possession of the practitioner with respect to the use, safety and efficacy of the new drug, the names of the institutions at which the new drug is to be used and such other information as may be requested by Health Canada. In addition, the practitioner must agree to report to both the drug manufacturer and Health Canada the results of the new drug's use in the medical emergency, including information concerning adverse reactions, and must account to Health Canada for all quantities of the new drug made available.

The Canadian regulatory approval requirements for new drugs outlined above are similar to those of other major pharmaceutical markets. While the testing carried out in Canada is often acceptable for the purposes of regulatory submissions in other countries, individual regulatory authorities may request supplementary testing during their assessment of any submission. Therefore, the clinical testing conducted under Health Canada authorization or the approval of regulatory authorities of other countries may not be accepted by regulatory authorities outside Canada or other countries.

### *Approval of New Drugs in the United States*

In the United States, the FDA controls and investigates the investigation, manufacturing, and sale of new drugs. New drugs require FDA approval of an NDA prior to commercial sale. In the case of certain biological products, a Biological License Application (“BLA”) must be obtained prior to marketing and batch releasing. As in Canada, to obtain marketing approval, data from adequate and well-controlled human clinical trials, demonstrating to the FDA’s satisfaction a new drug’s safety and effectiveness for its intended use, are required. Data are generated in studies conducted pursuant to an investigational new drug (“IND”) submission, similar to that required for a clinical trial application in Canada. Clinical trials with human subjects are characterized as Phase 1, Phase 2 and Phase 3 trials or a combination thereof. In a marketing application, the manufacturer must also demonstrate the identity, potency, quality and purity of the active ingredients of the new drug involved, and the stability of those ingredients. Further, the manufacturing facilities, equipment, processes and quality controls for the new drug must comply with the FDA’s current cGMP regulations for drugs both in a pre-licensing inspection before product licensing and in subsequent periodic inspections after licensing. An establishment license grants the sponsor permission to fabricate, package, label, distribute, import, wholesale or test the newly approved drug.

Federally regulated trials must be approved and monitored by an independent committee of doctors, scientists, advocates, and others to ensure safety and ethical standards, IRBs or ERBs. The review boards study and approve all study-related documents before a clinical trial begins and also carefully monitor data to detect benefit or harm, and validity of results.

### *Post-Approval Regulation*

The monitoring of a new drug does not cease once it is on the market. For example, a manufacturer of a new drug must report any new information received concerning serious side effects, as well as the failure of the new drug to produce desired effects. If Health Canada determines it to be in the interest of public health, a notice of compliance for a new drug may be suspended and the new drug may be removed from the market.

A post surveillance program involves clinical trials conducted after a drug is marketed (referred to as Phase 4 studies in the United States) and is an important source of information on as yet undetected adverse outcomes, especially in populations that may not have been involved in the premarketing trials (e.g., children, the elderly, pregnant women) and the drug’s long-term morbidity and mortality profile. Regulatory authorities may require companies to conduct Phase 4 studies as a condition of market approval. Companies often conduct post-marketing studies in the absence of a regulatory mandate.

The foregoing description is a summary of the requirements for a new drug to be approved for marketing in North America. The EMA and Japanese Pharmaceuticals and Medical Devices Agency are also important regulatory authorities in drug development. Together with the FDA, they are the three International Conference on Harmonization parties which oversee the three largest markets for drug sales.

### **Information About Our Executive Officers**

Aptose’s leadership team comprises accomplished industry, financial and clinical research professionals who are dedicated to building a comprehensive anticancer drug pipeline and clinical development programs focused on targeted therapeutics directed against dysregulated oncogenic processes in patients with life. The team includes our President, Chairman and Chief Executive Officer, our Chief Financial Officer, our Chief Medical Officer, and our Chief Commercial Officer.

*William G. Rice, Ph.D.*, age 63, joined Aptose as Chairman and Chief Executive Officer in October 2013. Dr. Rice brings 25 years of C-level experience in the biotech industry to Aptose. Prior to joining Aptose, Dr. Rice served as the President, Chief Executive Officer and Chairman of the board of Cylene Pharmaceuticals, Inc. (“Cylene”), a private biotechnology company, from 2003 to 2013. Prior to Cylene, Dr. Rice was the founder, President, Chief Executive Officer and Director of Achillion Pharmaceuticals, Inc. from 1998 to 2003. He also served as Senior Scientist and Head of the Drug Mechanism Laboratory at the National Cancer Institute-Frederick Cancer Research and Development Center from 1992 to 1998 and served as a faculty member in the division of Pediatric Hematology and Oncology at Emory University School of Medicine from 1989 to 1992. Dr. Rice received his Ph.D. from Emory University Department of Biochemistry.

*Fletcher Payne*, age 60, joined Aptose as Senior Vice President and Chief Financial Officer (“CFO”) in June 2022. With a healthcare tenure of more than two decades, Mr. Payne most recently served as CFO of Syapse, where he completed several financing transactions and oversaw accounting, finance, corporate development, and legal functions. Prior, he served as CFO at Catalyst Bioscience, a publicly traded biotech company. He served in a CFO capacity and senior financial positions at CytomX Therapeutics, Plexxikon Inc., Rinat Neuroscience Corporation, Dynavax Technologies Corporation, and Cell Genesys, among others. Mr. Payne holds a B.S. in Finance from the Haas School of Business, University of California, Berkeley.

*Rafael Bejar, M.D, Ph.D.*, age 51, joined Aptose as Senior Vice President and Chief Medical Officer in January 2020. Dr. Bejar is an internationally recognized physician scientist with extensive research and clinical experience in the area of hematologic malignancies. Dr. Bejar joined Aptose from UC San Diego (“UCSD”) where he began working in 2012. He continues to serve at UCSD as an Associate Professor of Clinical Medicine, caring for patients and maintaining a research laboratory focused on translational studies of myeloid malignancies and also serves and is an independent consultant as a member of the Independent Data Monitoring Committee for other pharmaceutical companies. At UCSD, he founded the MDS Center of Excellence and led the Hematology Disease Team from 2017 to 2019. There he has directed several clinical studies and served as an advisor for numerous companies including Celgene, Takeda, AbbVie, Astex, Genoptix, Forty Seven, PersImmune, and Daiichi-Sankyo. Outside UCSD, Dr. Bejar sits on the Scientific Advisory Board for the MDS Foundation, is a prior member of the National Comprehensive Cancer Network Guidelines Committee, and has led projects for the International Working Group for MDS. He is frequently invited to speak at national and international meetings and has published articles in a variety of journals including The New England Journal of Medicine, Journal of Clinical Oncology, Leukemia, Blood, and Blood Advances. Dr. Bejar completed his fellowship at the Dana-Farber Cancer Institute and has been board certified in Hematology and Oncology. He completed his internship in Internal Medicine at the University of Chicago followed by his residency at the Brigham and Women’s Hospital in Boston where he later served a Medical Chief Resident and an Instructor in Hematology. He holds an M.D. degree and Neuroscience Ph.D. from UCSD and a B.S. in Physics from MIT.

*Philippe Ledru*, age 56, joined Aptose as Senior Vice President and Chief Commercial Officer on April 7, 2022. Mr. Ledru brings to Aptose more than 30 years of pharmaceutical industry experience in the U.S. and Europe, including innovative drug development and commercial and strategic experience at two top global oncology companies. Most recently, he served as Associate Vice President and Head of Oncology New Products at Merck & Co, where he was responsible for commercial leadership over the entire Merck oncology pipeline, over 25 assets from discovery to mid-stage clinical development, across major solid tumors and hematological malignancies. At Merck, he also provided leadership on all licensing and M&A activities, including the Peloton Therapeutics and Arqule acquisitions in 2019. Prior, Mr. Ledru spent a 20+ year career at Novartis in the U.S. and France, most recently as Senior Director of Early Commercial Strategy focused on oncology products. There he also was part of the brand team and had early commercial development and global marketing responsibilities for several new compounds, including midostaurin. Earlier at Novartis Oncologie, he helped lead launches of several oncology products, including imatinib (Gleevec), a landmark drug that has greatly improved the outcomes of patients with chronic myelogenous leukemia. Mr. Ledru also held oncology product management and business development positions at Zeneca Pharma France/ICI Pharma.

## Corporate Information

Aptose is a publicly traded company governed by the CBCA. Our headquarters are located at 251 Consumers Road, Suite 1105 Toronto, Ontario, Canada M2J 4R3 (telephone: 647-479-9828), and our executive offices are located at 12770 High Bluff Drive, Suite 120, San Diego, CA 92130 (telephone: 858-926-2730).

We file annual, quarterly, current reports, proxy statements and other information with the SEC. The SEC maintains an Internet site that contains our public filings and other information regarding the Company, at [www.sec.gov](http://www.sec.gov). We make these reports available free of charge at our website <http://www.apptose.com> (under the “Investors — Financial Information” caption).

We are also a reporting issuer under the securities laws of every province of Canada.

## Cautionary Note Regarding Forward-Looking Statements and Risk Factor Summary

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995 and “forward-looking information” within the meaning of applicable Canadian securities law. We refer to such forward-looking statements and forward-looking information collectively as “forward-looking statements”. These statements relate to future events or future performance and reflect our expectations and assumptions regarding our growth, results of operations, performance and business prospects and opportunities. Such forward-looking statements reflect our current beliefs and are based on information currently available to us. In some cases, forward-looking statements can be identified by terminology such as “may”, “would”, “could”, “will”, “should”, “expect”, “plan”, “intend”, “anticipate”, “believe”, “estimate”, “predict”, “potential”, “continue” or the negative of these terms or other similar expressions concerning matters that are not historical facts. The forward-looking statements in this Annual Report on Form 10-K include, among others, statements regarding our future operating results, economic performance and product development efforts and statements in respect of:

- our ability to obtain the substantial capital we require to fund research and operations and to continue as a going concern;
- our business strategy;
- our clinical development plans;
- our plans to conduct clinical trials and preclinical programs;
- our ability to accrue appropriate numbers and types of patients;
- our reliance on external contract research/manufacturing organizations for certain activities;
- our plans to secure and maintain strategic partnerships to assist in the further development of our product candidates and to build our pipeline;
- our ability to file and maintain intellectual property to protect our pharmaceutical assets;
- potential exposure to legal actions and potential need to take action against other entities;
- our expectations regarding the progress and the successful and timely completion of the various stages of our drug discovery, drug synthesis and formulation, preclinical and clinical studies and the regulatory approval process;
- our plans, objectives, expectations, and intentions; and
- other statements including words such as “anticipate,” “contemplate,” “continue,” “believe,” “plan,” “estimate,” “expect,” “intend,” “will,” “should,” “may,” and other similar expressions.

The forward-looking statements contained in this Annual Report on Form 10-K reflect our current views with respect to future events, are subject to significant risks and uncertainties, and are 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. Forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K.



Except as required under applicable securities legislation, we undertake no obligation to publicly update or revise forward-looking statements, whether as a result of new information, future events or otherwise.

### ***Risk Factor Summary***

Many factors could cause our actual results, performance or achievements to be materially different from any future results, performance, or achievements that may be expressed or implied by such forward-looking statements, including, among others:

- our ability to continue as a going concern
- our lack of product revenues and net losses and a history of operating losses;
- our early stage of development, particularly the inherent risks and uncertainties associated with (i) developing new drug candidates generally, (ii) demonstrating the safety and efficacy of these drug candidates in clinical studies in humans, and (iii) obtaining regulatory approval to commercialize these drug candidates;
- our need to raise substantial additional capital in the future and that we may be unable to raise such funds when needed and on acceptable terms;
- further equity financing, which may substantially dilute the interests of our existing shareholders;
- clinical studies and regulatory approvals of our drug candidates are subject to delays, and may not be completed or granted on expected timetables, if at all, and such delays may increase our costs and could substantially harm our business;
- our reliance on external contract research/manufacturing organizations for certain activities and if we are subject to quality, cost, or delivery issues with the preclinical and clinical grade materials supplied by contract manufacturers, our business operations could suffer significant harm;
- clinical studies are long, expensive and uncertain processes and the FDA, or other similar foreign regulatory agencies that we are required to report to, may ultimately not approve any of our product candidates;
- Our operations could be adversely affected by events outside of our control, such as natural disasters, wars or health crises such as the COVID-19 pandemic.
- our ability to comply with applicable governmental regulations and standards;
- our inability to achieve our projected development goals in the time frames we announce and expect;
- difficulties in enrolling patients for clinical trials may lead to delays or cancellations of our clinical trials;
- our reliance on third-parties to conduct and monitor our preclinical studies;
- our ability to attract and retain key personnel, including key executives and scientists;
- any misconduct or improper activities by our employees;
- our exposure to exchange rate risk;
- our ability to commercialize our business attributed to negative results from clinical trials;
- the marketplace may not accept our products or product candidates due to the intense competition and technological change in the biotechnical and pharmaceuticals industries, and we may not be able to compete successfully against other companies in our industries and achieve profitability;
- our ability to obtain and maintain patent protection;
- our ability to afford substantial costs incurred with defending our intellectual property;
- our ability to protect our intellectual property rights and not infringe on the intellectual property rights of others;

- our business is subject to potential product liability and other claims;
- potential exposure to legal actions and potential need to take action against other entities;
- commercialization limitations imposed by intellectual property rights owned or controlled by third parties;
- our ability to maintain adequate insurance at acceptable costs;
- our ability to find and enter into agreements with potential partners;
- extensive government regulation;
- data security incidents and privacy breaches could result in increased costs and reputational harm;
- our share price has been and is likely to continue to be volatile;
- future sales of our Common Shares by us or by our existing shareholders could cause our share price to drop;
- changing global market and financial conditions;
- changes in an active trading market in our Common Shares;
- our ability to maintain listing of our Common Shares on the Nasdaq and / or TSX
- difficulties by non-Canadian investors to obtain and enforce judgments against us because of our Canadian incorporation and presence;
- potential adverse U.S. federal tax consequences for U.S. shareholders because we are a “passive foreign investment company”;
- our “smaller reporting company” status;
- any failures to maintain an effective system of internal controls may result in material misstatements of our financial statements, or cause us to fail to meet our reporting obligations or fail to prevent fraud;
- our broad discretion in how we use the proceeds of the sale of Common Shares;
- our ability to expand our business through the acquisition of companies or businesses; and
- other risks detailed from time-to-time in our on-going filings with the SEC and Canadian securities regulators, and those which are discussed in Item 1A. Risk Factors in this Annual Report on Form 10-K.

Should one or more of these risks or uncertainties materialize, or should the assumptions described in the Item 1A. Risk Factors in this Annual Report on Form 10-K underlying those forward-looking statements prove incorrect, actual results may vary materially from those described in the forward-looking statements.

Although we have attempted to identify factors that could cause actual actions, events or results to differ materially from those described in forward-looking statements, there may be other factors that cause actions, events or results not to be as anticipated, estimated or intended. Forward-looking statements are based upon our beliefs, estimates and opinions at the time they are made and we undertake no obligation to update forward-looking statements if these beliefs, estimates and opinions or circumstances should change, except as required by applicable law. There can be no assurance that forward-looking statements will prove to be accurate, as actual results and future events could differ materially from those anticipated in such statements. Accordingly, readers should not place undue reliance on forward-looking statements.

**We qualify all the forward-looking statements contained in this Annual Report on Form 10-K by the foregoing cautionary statements.**

## ITEM 1A. RISK FACTORS

### *Risk Factors and Uncertainties*

Any of the risks and uncertainties described below could significantly and negatively affect our business, prospects, financial condition, operating results, or credit ratings, which could cause the trading price of our Common Shares to decline. Additional risks and uncertainties not presently known to us, or risks that we currently consider immaterial, could also impair our business operations or financial condition. The following discussion of risk factors contains “forward-looking” statements, as discussed above.

### **Risks Related to our Business**

*There is substantial doubt that the company can remain a going concern over the next twelve months.*

Management recognizes that in order for us to meet our capital requirements, and continue to operate, additional financing will be necessary. We plan to raise additional funds in order to fund our business operations. We will seek access to financing but there is no assurance that such additional funds will be available for us to finance our operations on acceptable terms, if at all. These conditions raise substantial doubt about the Company’s ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Our ability to raise additional funds could be affected by adverse market conditions, the status of our product pipeline, possible delays in enrollment in our trial, and various other factors and we may be unable to raise capital when needed, or on terms favorable to us. If necessary funds are not available, we may have to delay, reduce the scope of, or eliminate some of our development programs, potentially delaying the time to market for any of our product candidates.

*We are an early-stage development company with no revenues from product sales.*

We are at an early stage of development. None of our potential products has obtained regulatory approval for commercial use and sale in any country and as such, no revenues have resulted from product sales. Significant additional investment will be necessary to complete the development of any of our product candidates. Preclinical and clinical trial work must be completed before our potential products could be ready for use within the markets that we have identified. We may fail to develop any products, obtain regulatory approvals, enter or complete clinical trials or commercialize any products. We do not know whether any of our potential product development efforts will prove to be effective, meet applicable regulatory standards, obtain the requisite regulatory approvals, be capable of being manufactured at a reasonable cost or be accepted in the marketplace.

The product candidates we are currently developing are not expected to be commercially viable for at least the next several years and we may encounter unforeseen difficulties or delays in commercializing our product candidates. In addition, our potential products may not be effective or may cause undesirable side effects.

Our product candidates require significant funding to reach regulatory approval assuming positive clinical results. We are currently conducting Phase 1 clinical trials with our product candidates tuspentinib and luxepatinib. Significant additional capital will be necessary to complete the Phase 1 clinical trials, and if required, Phase 2 or Phase 3 clinical trials. Such funding for our product candidates may be difficult, or impossible to raise in the public or private markets or through partnerships. If funding or partnerships are not readily attainable, the development of our product candidates may be significantly delayed or stopped altogether. The announcement of a delay or discontinuation of development of any of our product candidates could have a negative impact on our share price.

*We need to raise additional capital.*

We have an ongoing need to raise additional capital. To obtain the necessary capital, we must rely on some or all of the following: additional share issues, debt issuances (including promissory notes), collaboration agreements or corporate partnerships and grants and tax credits to provide full or partial funding for our activities. Additional funding may not be available on terms that are acceptable to us or in amounts that will enable us to carry out our business plan.

Our need for capital may require us to:

- engage in equity financings that could result in significant dilution to existing investors;
- delay or reduce the scope of or eliminate one or more of our development programs;
- obtain funds through arrangements with collaborators or others that may require us to relinquish rights to technologies, product candidates or products that we would otherwise seek to develop or commercialize ourselves;
- license rights to technologies, product candidates or products on terms that are less favorable to us than might otherwise be available;
- considerably reduce operations; or
- cease our operations.

In addition, sales of our Common Shares in the public markets, or the perception that such sales could occur, could depress the market price of our Common Shares and impair our ability to raise capital through the sale of additional equity securities.

***Our operations could be adversely affected by events outside of our control, such as natural disasters, wars or health crises such as the COVID-19 pandemic.***

We may be impacted by business interruptions resulting from pandemics and public health emergencies, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires. Any such event, or a fear of the foregoing, could adversely impact us by causing operating, manufacturing, supply chain, clinical trial and project development delays and disruptions, labor shortages, travel and shipping disruption or shutdowns. We may incur expenses or delays relating to such events outside of our control, which could have a material adverse impact on our business, operating results and financial condition.

***We have a history of operating losses. We expect to incur net losses and we may never achieve or maintain profitability.***

We have not been profitable since our inception in 1986. We reported net losses of \$41.8 million in the fiscal year ended December 31, 2022, \$65.4 million in the fiscal year ended December 31, 2021, \$55.2 million in the fiscal year ended December 31, 2020, and as of December 31, 2022, we had an accumulated deficit of \$464.3 million.

We have not generated any significant revenue to date and it is possible that we will never have sufficient product sales revenue (if any) to achieve profitability. We expect to continue to incur losses for at least the next several years as we or our collaborators and licensees pursue clinical trials and research and development efforts. To become profitable, we, either alone or with our collaborators and licensees, must successfully develop, manufacture and market our current product candidates tuspentinib or luxepitinib, as well as continue to identify, develop, manufacture and market new product candidates. It is possible that we will never have significant product sales revenue or receive royalties on our licensed product candidates. If funding is insufficient at any time in the future, we may not be able to develop or commercialize our products, take advantage of business opportunities or respond to competitive pressures.

We currently do not earn any revenues from our drug candidates and are therefore considered to be in the development stage. The continuation of our research and development activities and the commercialization of the targeted therapeutic products are dependent upon our ability to successfully finance and complete our research and development programs through a combination of equity financing and payments from strategic partners. We have no current sources of significant payments from strategic partners.

***We heavily rely on the capabilities and experience of our key executives and scientists and the loss of any of them could affect our ability to develop our products.***

The loss of our executive officers could harm our operations and our ability to achieve strategic objectives. While we have employment agreements with our executive officers, such employment agreements do not guarantee their retention. We also depend on our scientific and clinical collaborators and advisors, all of whom have outside commitments that may limit their availability to us. In addition, we believe that our future success will depend in large part upon our ability to attract and retain highly skilled scientific, managerial, medical, clinical and regulatory personnel, particularly as we expand our activities and seek regulatory approvals for clinical trials. We routinely enter into consulting agreements with our scientific and clinical collaborators and advisors, key opinion leaders and academic partners in the ordinary course of our business. We also enter into contractual agreements with physicians and institutions who will recruit patients into our clinical trials on our behalf in the ordinary course of our business. Notwithstanding these arrangements, we face significant competition for these types of personnel from other companies, research and academic institutions, government entities and other organizations. We cannot predict our success in hiring or retaining the personnel we require for continued growth. The loss of the services of any of our executive officers or other key personnel could potentially harm our business, operating results or financial condition.

***Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include failures to comply with FDA/Health Canada regulations, provide accurate information to the FDA/Health Canada, comply with manufacturing standards we have established, comply with federal, state and provincial health-care fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a substantial impact on our business and results of operations, including the imposition of substantial fines or other sanctions.

***We have no sales, marketing or distribution experience and would have to invest significant financial and management resources to establish these capabilities.***

We have no sales, marketing or distribution experience. We currently expect to rely heavily on third parties to launch and market our products, if they are approved. However, if we elect to develop internal sales, distribution and marketing capabilities, we will need to invest significant financial and management resources. For products where we decide to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including:

- we may not be able to attract and build a significant marketing or sales force;
- the cost of establishing a marketing or sales force may not be justifiable in light of the revenues generated by any particular product; and
- our direct sales and marketing efforts may not be successful.

If we are unable to develop our own sales, marketing and distribution capabilities, we will not be able to successfully commercialize our products without reliance on third parties.

***We may expand our business through the acquisition of companies or businesses or by entering into collaborations or by in-licensing product candidates, each of which could disrupt our business and harm our financial condition.***

We may seek to expand our pipeline and capabilities by acquiring one or more companies or businesses, entering into collaborations or in-licensing one or more product candidates. For example, in June 2016, we entered into a definitive agreement with CG, granting Aptose an exclusive option to research, develop and commercialize CG-806 in all countries of the world except Korea, for all fields of use, and in November 2021 we entered into an agreement with Hanmi granting Aptose exclusive worldwide rights to develop and commercialize tuspetinib.

Acquisitions, collaborations and in-licenses involve numerous risks, including, but not limited to:

- substantial cash expenditures;
- technology development risks;
- potentially dilutive issuances of equity securities;
- incurrence of debt and contingent liabilities, some of which may be difficult or impossible to identify at the time of acquisition;
- difficulties in assimilating the operations of the acquired companies;
- potential disputes regarding contingent consideration;
- diverting our management’s attention away from other business concerns;
- entering markets in which we have limited or no direct experience;
- potential loss of our key employees or key employees of the acquired companies or businesses; and
- failure of the in-licenses agents or technologies to deliver the desired activities or functions.

We have experience in entering collaborations and in-licensing product candidates; however, we cannot provide assurance that any acquisition, collaboration or in-license will result in any benefit to us. We may incorrectly judge the value or worth of an acquired company or business or in-licensed product candidate. In addition, our future success could depend in part on our ability to manage the rapid growth associated with some of these acquisitions, collaborations and in-licenses. We cannot assure you that we would be able to successfully combine our business with that of acquired businesses, manage a collaboration or integrate in-licensed product candidates. Furthermore, the development or expansion of our business may require a substantial capital investment by us.

***Fluctuations in exchange rates can cause us to incur losses.***

We may be exposed to fluctuations of the U.S. dollar against certain other currencies because we hold most of our cash and cash equivalents in U.S. dollars, while we incur some of our expenses in foreign currencies, primarily the Canadian dollar. Fluctuations in the value of currencies could cause us to incur currency exchange losses, and we do not currently employ a hedging strategy against exchange rate risk. As a result, changes in the exchange rate between the Canadian dollar and the U.S. dollar could materially impact our reported results of operations and distort period to period comparisons. In particular, to the extent that foreign currency-denominated (i.e., non-U.S. dollar) monetary assets do not equal the amount of our foreign currency denominated monetary liabilities, foreign currency gains or losses could arise and materially impact our financial statements. As a result of such foreign currency fluctuations, it could be more difficult to detect underlying trends in our business and results of operations. In addition, to the extent that fluctuations in currency exchange rates cause our results of operations to differ from our expectations or the expectations of our investors, the trading price of our Common Shares could be adversely affected.

## **Risks Related to Development, Clinical Testing and Regulatory Approval of Our Product Candidates**

### ***Fast Track Designation by the FDA may not lead to a faster development or regulatory review or approval process.***

We have obtained Fast Track Designation for HM43239 for the treatment of patients with R/R AML and FLT3 mutation. We may seek Fast Track Designation for one or more of our other product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

### ***Clinical trials are long, expensive and uncertain processes and the FDA or Health Canada may ultimately not approve any of our product candidates. We may never develop any commercial drugs or other products that generate revenues.***

None of our product candidates has received regulatory approval for commercial use and sale in North America. We cannot market a pharmaceutical product in any jurisdiction until it has completed thorough preclinical testing and clinical trials in addition to that jurisdiction's extensive regulatory approval process. Approval in one country does not assure approval in another country. In general, significant research and development and clinical studies are required to demonstrate the safety and efficacy of our product candidates before we can submit any applications for regulatory approval.

Clinical trials are long, expensive and uncertain processes. Clinical trials may not start or be on schedule and the FDA, Health Canada or any other regulatory body may not ultimately approve our product candidates for commercial sale in the relevant territory. The clinical trials of any of our drug candidates could be unsuccessful, which would prevent us from advancing, commercializing or partnering the drug.

Even if the results of our preclinical studies or clinical trials are initially positive, it is possible that we will obtain different results in the later stages of drug development or that results seen in clinical trials will not continue with longer term treatment. Positive results in Phase 1 clinical trials may not necessarily repeat in larger Phase 2 or Phase 3 clinical trials.

Our preclinical studies and clinical trials may not generate positive results that will allow us to move towards the commercial use and sale of our product candidates. Furthermore, negative preclinical or clinical trial results may cause our business, financial condition, or results of operations to be materially adversely affected. Our tuspetinib and luxepitinib product candidates are currently being evaluated in Phase 1 studies, and are expected to undergo many years of testing and regulatory examinations prior to any potential regulatory approvals.

Preparing, submitting and advancing applications for regulatory approval of products is complex, expensive and time intensive and entails significant uncertainty. A commitment of substantial resources to conduct time-consuming research, preclinical studies and clinical trials is required if we are to complete development of our products.

Clinical trials of our products require that we identify and enroll a large number of patients with the illness under investigation. We may not be able to enroll a sufficient number of appropriate patients to complete our clinical trials in a timely manner, particularly in smaller indications and indications where there is significant competition for patients. If we experience difficulty in enrolling a sufficient number of patients to conduct our clinical trials, we may need to delay or terminate ongoing clinical trials and will not accomplish objectives material to our success. Delays in planned patient enrollment or lower than anticipated event rates in our current clinical trials or future clinical trials also may result in increased costs, program delays, or both.

In addition, unacceptable toxicities or adverse side effects may occur at any time in the course of preclinical studies or human clinical trials or, if any product candidates are successfully developed and approved for marketing, during commercial use of any approved products. The appearance of any unacceptable toxicities or adverse side effects could interrupt, limit, delay or abort the development of any of our product candidates or, if previously approved, necessitate their withdrawal from the market. Furthermore, disease resistance or other unforeseen factors may limit the effectiveness of our potential products.

Our failure to develop safe and commercially viable drugs would substantially impair our ability to generate revenues and sustain our operations and would materially harm our business and adversely affect our share price.

***We may choose to expend our limited resources on programs that do not yield successful product candidates as opposed to indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited resources and access to capital to fund our operations, our management must make strategic decisions as to which product candidates and indications to pursue and how much of our resources to allocate to each. Our management must also evaluate the benefits of developing in-licensed or jointly owned technologies, which in some circumstances we may be contractually obligated to pursue, relative to developing other product candidates, indications or programs. Our management has broad discretion to suspend, scale down, or discontinue any or all of these development efforts, or to initiate new programs to treat other diseases. If we select and commit resources to opportunities that we are unable to successfully develop, or we forego more promising opportunities, our business, financial condition and results of operations will be adversely affected.

***We may not achieve our projected development goals in the time frames we announce and expect.***

We set goals for, and make public statements regarding, the expected timing of the accomplishment of objectives material to our success, such as the commencement and completion of clinical trials, the submission of a drug-regulatory application, and the expected costs to develop our product candidates. The actual timing and costs of these events can vary dramatically due to factors within and beyond our control, such as delays or failures in our IND submissions or clinical trials, issues related to the manufacturing of drug supply, uncertainties inherent in the regulatory approval process, market conditions and interest by partners in our product candidates, among other things. Our clinical trials may not be completed, we may not make regulatory submissions or receive regulatory approvals as planned; or we may not secure partnerships for any of our product candidates. Any failure to achieve one or more of these milestones as planned would have a material adverse effect on our business, financial condition and results of operations.

***Delays in clinical testing could result in delays in commercializing our product candidates and our business may be substantially harmed.***

We cannot predict whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, if at all. Our product development costs will increase if we experience delays in clinical testing. Significant clinical trial delays could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before us, which would impair our ability to successfully commercialize our product candidates and may harm our financial condition, results of operations and prospects. The completion of clinical trials for our products, including the tuspentinib and luxetpinib clinical trials may be delayed for a number of reasons, including delays related, but not limited, to:

- failure by regulatory authorities to grant permission to proceed with a clinical trial;
- a regulatory decision to place or placing the clinical trial on hold;
- patients failing to enroll or remain in our trials at the rate we expect;
- suspension or termination of clinical trials by regulators for many reasons, including concerns about patient safety or failure of our contract manufacturers to comply with cGMP requirements;
- any changes to our manufacturing process that may be necessary or desired;



- delays or failure to obtain GMP-grade clinical supply from contract manufacturers of our products necessary to conduct clinical trials;
- product candidates demonstrating a lack of safety or efficacy during clinical trials;
- patients choosing an alternative treatment for the indications for which we are developing any of our product candidates or participating in competing clinical trials;
- patients failing to complete clinical trials due to dissatisfaction with the treatment, side effects or other reasons;
- reports of clinical testing on similar technologies and products raising safety and/or efficacy concerns;
- competing clinical trials and scheduling conflicts with participating clinicians;
- clinical investigators not performing our clinical trials on their anticipated schedule, dropping out of a trial, or employing methods not consistent with the clinical trial protocol, regulatory requirements or other third parties not performing data collection and analysis in a timely or accurate manner;
- failure of our contract research organizations, or CROs, to satisfy their contractual duties or meet expected deadlines;
- inspections of clinical trial sites by regulatory authorities or IRBs, or ethics committees or boards finding regulatory violations that require us to undertake corrective action, resulting in suspension or termination of one or more sites or the imposition of a clinical hold on the entire study;
- one or more IRBs or ethics committees or boards rejecting, suspending or terminating the study at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial; or
- failure to reach agreement on acceptable terms with prospective clinical trial sites.

Our product development costs will increase if we experience delays in testing or approval or if we need to perform more or larger clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur, and we may need to amend study protocols to reflect these changes. Amendments may require us to resubmit our study protocols to regulatory authorities or IRBs or ethics committees or boards for re-examination, which may impact the cost, timing or successful completion of a trial. Delays or increased product development costs may have a material adverse effect on our business, financial condition and prospects.

***We rely on contract manufacturers over whom we have limited control. If we are subject to quality, cost or delivery issues with the preclinical and clinical grade materials supplied by contract manufacturers, our business operations could suffer significant harm.***

We rely on CMOs to manufacture our product candidates for some preclinical studies and clinical trials. We rely on CMOs for manufacturing, filling, packaging, storing and shipping of drug product in compliance with cGMP regulations applicable to our products. The FDA and other regulatory agencies ensure the quality of drug products by carefully monitoring drug manufacturers' compliance with cGMP regulations. The cGMP regulations for drugs contain minimum requirements for the methods, facilities and controls used in manufacturing, processing and packing of a drug product.

We contracted with multiple CMOs for the manufacture of tuspetinib and luxepitinib to supply the active ingredient and then drug product for our clinical trials. The synthesis of luxepitinib is challenging from a scale-up synthetic chemistry perspective. We pre-qualified CMOs to have the capacity, the systems and the experience to supply tuspetinib and luxepitinib for our clinical trials. We have qualified the manufacturing facilities and the FDA has also performed site audits for our selected CMOs. In spite of the efforts to prequalify CMOs, delays and errors may occur, and any such manufacturing failures, delays or compliance issues could cause delays in the completion of our clinical trial programs.

There can be no assurances that CMOs will be able to meet our timetable and requirements. We have contracted with alternate suppliers in the event our current CMOs are unable to scale up production, or if our current CMOs otherwise experience any other significant problems in the manufacture of tucatinib and luxetatinib. However, it is possible that all third-party manufacturing sources may experience failure or delays and may demand commercially unreasonable terms, which may lead to further delays in the development of our product candidates. Further, contract manufacturers must operate in compliance with cGMP and failure to do so could result in, among other things, the disruption of product supplies. Our dependence upon third parties for the manufacture of our products may adversely affect our profit margins and our ability to develop and deliver products on a timely and competitive basis.

***Some components of our products are manufactured by third parties outside of the United States, and our business may be harmed by legal, regulatory, economic, political and public health risks associated with international trade and those markets.***

We have third-party manufacturing partners in South Korea, Germany and the United Kingdom; in addition, some materials used by our third-party manufacturers are supplied by companies located in other countries, including China. Our reliance on suppliers and manufacturers in foreign markets creates risks inherent in doing business in foreign jurisdictions, including: (a) the burdens of complying with a variety of foreign laws and regulations, including laws relating to the importation and taxation of goods (b) public health crises, such as pandemics and epidemics, in the countries where our suppliers and manufacturers are located; (c) transportation interruptions or increases in transportation costs; and (d) foreign intellectual property infringement risks.

***If we have difficulty enrolling patients in clinical trials, the completion of the trials may be delayed or canceled.***

As our product candidates advance from preclinical testing to clinical testing, and then through progressively larger and more complex clinical trials, we will need to enroll an increasing number of patients that meet our eligibility criteria. There is significant competition for recruiting cancer patients in clinical trials, and we may be unable to enroll the patients we need to complete clinical trials for cancer indications on a timely basis or at all. Certain factors that affect enrollment of patients in our clinical trials are impacted by external forces that may be beyond our control. Such factors include, but are not limited to, the following:

- size and nature of the patient population;
- eligibility and exclusion criteria for the trial;
- design of the study protocol;
- competition with other companies for clinical sites or patients;
- the perceived risks and benefits of the product candidate under study;
- the patient referral practices of physicians; and
- the number, availability, location and accessibility of clinical trial sites.

Although, as of the date of this report, we do not foresee material delays to the enrollment of patients or timelines for our trials due to COVID-19, the extent to which COVID-19 will impact the projected development goals will depend on future developments, which are highly uncertain and cannot be predicted.

***If we are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience significant delays in doing so, we may not achieve marketing approval or realize the full commercial potential of our therapeutic product candidates.***

We plan to develop companion diagnostics for our therapeutic product candidates. We expect that, at least in some cases, regulatory authorities may require the development and regulatory approval of a companion diagnostic as a condition to approving our therapeutic product candidates. We have limited experience and capabilities in developing or commercializing diagnostics and plan to rely in large part on third parties to perform these functions. We do not currently have any agreement in place with any third party to develop or commercialize companion diagnostics for any of our therapeutic product candidates.

Companion diagnostics are subject to regulation by the FDA, Health Canada and comparable foreign regulatory authorities as medical devices and may require separate regulatory approval or clearance prior to commercialization. If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience delays in doing so, our business may be substantially harmed.

***We rely and will continue to rely on third parties to conduct and monitor many of our preclinical studies and our clinical trials, and their failure to perform as required could cause substantial harm to our business.***

We rely and will continue to rely on third parties to conduct a significant portion of our preclinical and clinical development activities. Preclinical activities include *in vivo* studies providing access to specific disease models, pharmacology and toxicology studies, and assay development. Clinical development activities include trial design, regulatory submissions, clinical patient recruitment, clinical trial monitoring, clinical data management and analysis, safety monitoring and project management, contract manufacturing and quality assurance. If there is any dispute or disruption in our relationship with third parties, or if they are unable to provide quality services in a timely manner and at a feasible cost, our active development programs will face delays. Further, if any of these third parties fails to perform as we expect or if their work fails to meet regulatory requirements, our testing could be delayed, canceled or rendered ineffective.

***Negative results from clinical trials or studies of others and adverse safety events involving the targets of our products may have an adverse impact on our future commercialization efforts.***

From time to time, studies or clinical trials on various aspects of biopharmaceutical products are conducted by academic researchers, competitors or others. The results of these studies or trials, when published, may have a significant effect on the market for the biopharmaceutical product that is the subject of the study. The publication of negative results of studies or clinical trials or adverse safety events related to our product candidates, or the therapeutic areas in which our product candidates compete, could adversely affect our share price and our ability to finance future development of our product candidates, and our business and financial results could be materially and adversely affected.

***The design or our execution of clinical trials may not support regulatory approval.***

The design or execution of a clinical trial can determine whether its results will support regulatory approval and flaws in the design or execution of a clinical trial may not become apparent until the clinical trial is well advanced. In some instances, there can be significant variability in safety or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any Phase 2, Phase 3 or other clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

Further, the FDA, Health Canada and comparable foreign regulatory authorities will have some discretion in the approval process and in determining when or whether regulatory approval will be obtained for any of our product candidates. Our product candidates may not be approved even if they achieve their primary endpoints in future Phase 3 clinical trials or registration trials. The FDA, Health Canada or other regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal Phase 3 clinical trial that has the potential to result in approval by the FDA, Health Canada or another regulatory agency. In addition, any of these regulatory authorities may also approve a product candidate for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. The FDA, Health Canada or other regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our product candidates.

*As a result of intense competition and technological change in the biotechnical and pharmaceutical industries, the marketplace may not accept our products or product candidates, and we may not be able to compete successfully against other companies in our industry and achieve profitability.*

Many of our competitors have:

- drug products that have already been approved or are in development;
- large, well-funded research and development programs in the biotechnical and pharmaceutical fields;
- substantially greater financial, technical and management resources, stronger intellectual property positions and greater manufacturing, marketing and sales capabilities, areas in which we have limited or no experience; and / or
- significantly greater experience than we do in undertaking preclinical testing and clinical trials of new or improved pharmaceutical products and obtaining required regulatory approvals.

Consequently, our competitors may obtain FDA, Health Canada and other regulatory approvals for product candidates sooner and may be more successful in manufacturing and marketing their products than we or our collaborators are.

Our competitors' existing and future products, therapies and technological approaches will compete directly with the products we seek to develop. Current and prospective competing products may be more effective than our existing and future products insofar as they may provide greater therapeutic benefits for a specific problem or may offer easier delivery or comparable performance at a lower cost.

For tuspentinib and luxetpinib in AML, examples of companies that have developed or are pursuing different therapies include Jazz (VYXEOS), Pfizer (MYLOTARG), Novartis (RYDAPT), Astellas (XOSPATA), AbbVie (VENCLEXTA), Daiichi Sankyo (quizartinib), Arog (crenolanib), Agios/Servier (TIBSOVO), Rigel (REZLIDHA), Celgene/BMS (IDHIFA), Kronos Bio (lanraplenib), Curis (emavusertib), Syndax (revumenib, SNDX-5613), and Kura (KO-539), among others.

For luxetpinib in B cell malignancies, examples of companies that have developed or are pursuing different approaches to BTK inhibition, both for the wild type and to the C481S-mutant forms, include AbbVie (IMBRUVICA), AstraZeneca (CALQUENCE), Beigene Co., Ltd. (Zanubrutinib), Merck (nemtabrutinib), and Eli Lilly (pirtobrutinib), among others.

Any product candidate that we develop and that obtains regulatory approval must then compete for market acceptance and market share. Our products may not gain market acceptance among physicians, patients, healthcare payers, insurers, the medical community and other stakeholders. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our product candidates for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

Further, any products we develop may become obsolete or face generic entry before we recover any expenses we incurred in connection with the development of these products. As a result, we may never achieve profitability.

## Risks Related to our Intellectual Property

*We may be unable to obtain patents to protect our technologies from other companies with competitive products, and patents of other companies could prevent us from manufacturing, developing or marketing our products.*

### *Patent protection*

The patent positions of pharmaceutical and biotechnology companies are uncertain and involve complex legal and factual questions. The United States Patent and Trademark Office (“USPTO”) and many other patent offices in the world have not established a consistent policy regarding the breadth of claims that they will allow in biotechnology patents.

Our pending patent applications may not result in issued patents and our issued patents may not be held valid and enforceable if challenged. Competitors may be able to circumvent any such issued patents by adoption of a competitive, though non-infringing product or process. Interpretation and evaluation of pharmaceutical or biotechnology patent claims present complex and often novel legal and factual questions. Our business could be adversely affected by increased competition in the event that any patent granted to it is held to be invalid or unenforceable or is inadequate in scope to protect our operations.

Allowable patentable subject matter and the scope of patent protection obtainable may differ between jurisdictions. If a patent office allows broad claims, the number and cost of patent interference proceedings in the United States, or analogous proceedings in other jurisdictions and the risk of infringement litigation may increase. If it allows narrow claims, the risk of infringement may decrease, but the value of our rights under our patents, licenses and patent applications may also decrease.

The scope of the claims in a patent application can be significantly modified during prosecution before the patent is issued. Consequently, we cannot know whether our pending applications will result in the issuance of patents or, if any patents are issued, whether they will provide us with significant proprietary protection or will be circumvented, invalidated or found to be unenforceable.

Publication of discoveries in scientific or patent literature often lags behind actual discoveries. Patent applications filed in the United States generally will be published 18 months after the filing date unless the applicant certifies that the invention will not be the subject of a foreign patent application. In many other jurisdictions, such as Canada, patent applications are published 18 months from the priority date. We may not be aware of such literature. Accordingly, we cannot be certain that the named inventors of our products and processes were the first to invent that product or process or that we were the first to pursue patent coverage for our inventions.

In addition, United States patent laws may change which could prevent or limit us from filing patent applications or patent claims in the United States to protect our products and technologies or limit the exclusivity periods that are available to patent holders for United States patents. For example, the Leahy-Smith America Invents Act, (the “Leahy-Smith Act”) was signed into law in 2011 and includes a number of significant changes to United States patent law. These include changes to transition from a “first-to-invent” system to a “first-to-file” system and to the way issued patents are challenged. These changes may favor larger and more established companies that have more resources to devote to patent application filing and prosecution. It is not clear what, if any, impact the Leahy-Smith Act will ultimately have on the cost of prosecuting our patent applications in the United States, our ability to obtain patents in the United States based on our discoveries and our ability to enforce or defend our United States issued patents.

Until such time, if ever, that further patents are issued to us, we will rely upon the law of trade secrets to the extent possible given the publication requirements under international patent treaty laws and/or requirements under foreign patent laws to protect our technology and our products incorporating the technology. In this regard, we have adopted certain confidentiality procedures. These include: limiting access to confidential information to certain key personnel; requiring all directors, officers, employees and consultants and others who may have access to our intellectual property to enter into confidentiality agreements which prohibit the use of or disclosure of confidential information to third parties; and implementing physical security measures designed to restrict access to such confidential information and products. Our ability to maintain the confidentiality of our technology is crucial to our ultimate possible commercial success. The procedures adopted by us to protect the confidentiality of our technology may not be effective, third parties may gain access to our trade secrets or our trade secrets or those of our collaborators may be independently discovered by others. Our collaborators, employees and consultants and other parties may not comply with the terms of their agreements with us, and we might be unable to adequately enforce our rights or obtain adequate compensation for the damages caused by unauthorized disclosure or use of our trade secrets or know how. Further, by seeking patent protection in various countries, it is inevitable that a substantial portion of our technology will become available to our competitors, through publication of such patent applications.

#### *Enforcement of intellectual property rights*

Protection of the rights revealed in published patent applications can be complex, costly and uncertain. Our commercial success depends in part on our ability to maintain and enforce our proprietary rights. If third parties engage in activities that infringe our proprietary rights, our management's focus will be diverted and we may incur significant costs in asserting our rights. We may not be successful in asserting our proprietary rights, which could result in our patents being held invalid or a court holding that the third party is not infringing, either of which would harm our competitive position.

Others may design around our patented technology. We may have to participate in interference proceedings declared by the USPTO, European opposition proceedings, or other analogous proceedings in other parts of the world to determine priority of invention and the validity of patent rights granted or applied for, which could result in substantial cost and delay, even if the eventual outcome is favorable to us. Our pending patent applications, even if issued, may not be held valid or enforceable.

#### ***Our products and product candidates may infringe the intellectual property rights of others, or others may infringe on our intellectual property rights which could increase our costs.***

Our success also depends on avoiding infringement of the proprietary technologies of others. In particular, there may be certain issued patents and patent applications claiming subject matter which we or our collaborators may be required to license in order to research, develop or commercialize tuspetinib or luxetinib. In addition, third parties may assert infringement or other intellectual property claims against us. An adverse outcome in these proceedings could subject us to significant liabilities to third-parties, require disputed rights to be licensed from third-parties or require us to cease or modify our use of the technology. If we are required to license third-party technology, a license under such patents and patent applications may not be available on acceptable terms or at all. Further, we may incur substantial costs defending ourselves in lawsuits against charges of patent infringement or other unlawful use of another's proprietary technology. We may also need to bring claims against others who we believe are infringing our rights in order to become or remain competitive and successful. Any such claims can be time consuming and expensive to pursue.

#### ***We may incur substantial cost in defending our intellectual property.***

While we believe that our products and technology do not infringe proprietary rights of others, third parties may assert infringement claims in the future and such claims could be successful. Even if challenges are unsuccessful, we could incur substantial costs in defending ourselves against patent infringement claims brought by others or in prosecuting suits against others. In addition, others may obtain patents that we would need to license, which may not be available to us on reasonable terms. Whether we are able to obtain a necessary license would depend on the terms offered, the degree of risk of infringement and the need for the patent.

***We have licensed important portions of our intellectual property from Hanmi and CG, and are subject to significant obligations under those license agreements.***

The Rights we hold under our license agreement with Hanmi and CG are critical to our business.

Our tuspetinib program is built around patents exclusively in-licensed from Hanmi, which permit us to research, develop and commercialize tuspetinib worldwide. Under our agreement with Hanmi, we are subject to significant obligations, including diligence obligations with respect to development and commercialization activities, payment obligations upon achievement of certain milestones and royalties on product sales, as well as other material obligations. Hanmi is eligible for payments upon the achievement of developmental, regulatory and commercial-based milestones, as well as tiered royalties on product sales.

Our luxetpinib program is built around patents exclusively in-licensed from CG, which permit us to research, develop and commercialize luxetpinib worldwide except for the Republic of Korea. Under our agreement with CG, we are subject to significant obligations, including diligence obligations with respect to development and commercialization activities, payment obligations upon achievement of certain milestones and royalties on product sales, as well as other material obligations. CG is eligible for payments upon the achievement of developmental, regulatory and commercial-based milestones, as well as low single-digit royalties on product sales.

If there is any conflict, dispute, disagreement or issue of non-performance between us and Hanmi or CG regarding our rights or obligations under the respective license agreements, including any conflict, dispute or disagreement arising from our failure to satisfy diligence or payment obligations under such agreements, Hanmi or CG may have a right to terminate the respective license. The loss of this license agreement could materially and adversely affect our ability to use intellectual property that could be critical to our drug discovery and development efforts, as well as our ability to enter into future collaboration, licensing and/or marketing agreements for one or more affected drug candidates or development programs.

***Our business depends, in part, on our ability to use technology that we have licensed or will in the future license from third parties, including CG, and, if these licenses were terminated or if we were unable to license additional technology we may need in the future, our business will be adversely affected.***

We currently hold licenses for certain technologies that are or may be critical to our current and subsequent product candidates. These include our exclusive license to research, develop and commercialize luxetpinib worldwide except for the Republic of Korea, and our exclusive license to develop and commercialize tuspetinib worldwide. Both licenses are subject to termination in the event of a breach by us of the license, if we fail to cure the breach following notice and the passage of a cure period. We may need to acquire additional licenses in the future to technologies developed by others. Furthermore, future license agreements may require us to make substantial milestone payments. We may also be obligated to make royalty payments on the sales, if any, of products resulting from the license. The termination of a license or the inability to license future technologies on acceptable terms may adversely affect our ability to develop or sell our products.

#### **Legal and Regulatory Risk**

***Our ability to develop, produce and market our products is subject to extensive government regulation.***

Government regulation is a significant factor in the development, production and marketing of our products. Research and development, testing, manufacture, marketing and sales of pharmaceutical products or related products are subject to extensive regulatory oversight, often in multiple jurisdictions, which may cause significant additional costs and/or delays in bringing products to market, and in turn, may cause significant losses to investors. The regulations applicable to our product candidates in a given jurisdiction may change. Even if granted, regulatory approvals may include significant limitations on the uses for which products can be marketed or may be conditioned on the conduct of post-marketing surveillance studies. Failure to comply with applicable regulatory requirements can, among other things, result in delay in approving or refusal to approve a product candidate, interruptions of clinical trials or manufacturing, suspension or withdrawal of regulatory approval, warning letters, the imposition of civil penalties or other monetary payments, product recall or seizure, operating restrictions, injunctions or criminal prosecution. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

Requirements for regulatory approval vary widely from country to country. Whether or not approved in Canada or the United States, regulatory authorities in other countries must approve a product prior to the commencement of marketing the product in those countries. The time required to obtain any such approval may be longer or shorter than in Canada or the United States. Approved drugs, as well as their manufacturers, are subject to continuing and ongoing review, and discovery of problems with these products or the failure to adhere to manufacturing or quality control requirements may result in regulatory restrictions being imposed.

***Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may adversely affect the prices we may obtain.***

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post approval activities and affect our ability to profitably sell any products for which we obtain marketing approval.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or collectively the Affordable Care Act, was enacted to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Additionally, the Drug Supply Chain Security Act, enacted in 2013, imposed new obligations on manufacturers of pharmaceutical products related to product tracking and tracing.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future. On June 17, 2021, the United States Supreme Court dismissed the most recent judicial challenge to the Affordable Care Act without specifically ruling on the constitutionality of the Affordable Care Act. Prior to the Supreme Court's decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the Affordable Care Act and our business.

We expect ongoing initiatives in the United States and internationally to increase pressure on drug pricing. Regulations that mandate price controls and limitations on patient access to products or establish prices paid by government entities or programs may impact product candidates that we may successfully develop. Pharmaceutical product pricing is subject to enhanced government and public scrutiny and calls for reform. Some U.S. states have implemented, and other U.S. states are considering, pharmaceutical price controls or patient access constraints under the Medicaid program, and some U.S. states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid eligible. Efforts by government officials or legislators to implement measures to regulate prices or payments for pharmaceutical products, including legislation on drug importation, could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop drug candidates.

Legislative and regulatory proposals have also been made to expand post approval requirements and restrict sales and promotional activities for pharmaceutical products in the US. Any healthcare reforms enacted in the future may, like the Affordable Care Act, be phased in over a number of years but, if enacted, could reduce our revenue, increase our costs, or require us to revise the ways in which we conduct business or put us at risk for loss of business. We are not sure whether additional legislative changes will be enacted, or whether the current regulations, guidance or interpretations will be changed, or what the impact of such changes on our business, if any, may be.



In Canada, the Patented Medicine Prices Review Board (“PMPRB”) has jurisdiction to control prices of patented medicines that are considered excessive. Recent changes to the regulations governing the PMPRB are intended to lower the prices of patented medicines even further. The PMPRB’s jurisdiction could extend to any of our drug products that are approved in Canada and protected under Canadian patents, with an adverse effect on the prices that we would otherwise obtain for these drugs in the relevant market.

***Coverage and adequate reimbursement may not be available for our product candidates, which could make it difficult for us to sell our products profitably.***

Market acceptance and sales of any drug candidates that we develop will depend in part on the extent to which reimbursement for these products and related treatments will be available from third party payors, including government health administration authorities and private health insurers. Third party payors decide which drugs they will pay for and establish reimbursement levels. Third party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for each of our drug candidates will be made on a plan by plan basis. One payor’s determination to provide coverage for a product does not assure that other payors will also provide coverage, and adequate reimbursement, for the product. Additionally, a third-party payor’s decision to provide coverage for a drug does not imply that an adequate reimbursement rate will be approved. Each plan determines whether or not it will provide coverage for a drug, what amount it will pay the manufacturer for the drug, and on what tier of its formulary the drug will be placed. The position of a drug on a formulary generally determines the copayment that a patient will need to make to obtain the drug and can strongly influence the adoption of a drug by patients and physicians. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Third party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage and reimbursement may impact the demand for, or the price of, any product for which we obtain marketing approval. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize any drug candidates that we develop.

Additionally, there have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions, including Canada, that could affect our ability to sell any future drugs profitably. These legislative and regulatory changes may negatively impact the reimbursement for any future drugs, following approval.

***We are subject to U.S. and Canadian healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations and diminished profits and future earnings.***

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with healthcare providers, patients and third-party payors could expose us to broadly applicable U.S. and Canadian laws and regulations relating to fraud abuse and healthcare more generally that may constrain the business or financial arrangements and collaborative partners through which we market, sell and distribute any products for which we obtain marketing approval.

Efforts to ensure that our collaborations with third parties, and our business generally, will comply with applicable U.S. and Canadian healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, contractual damages, reputational harm, disgorgement, curtailment or restricting of our operations, any of which could substantially disrupt our operations and diminish our profits and future earnings. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations.

***If product liability, clinical trial liability or environmental liability claims are brought against us or we are unable to obtain or maintain product liability, clinical trial or environmental liability insurance, we may incur substantial liabilities that could reduce our financial resources.***

The clinical testing and commercial use of pharmaceutical products involves significant exposure to product liability, clinical trial liability, environmental liability and other risks that are inherent in the testing, manufacturing and marketing of our products. These liabilities, if realized, could have a material adverse effect on our business, results of operations and financial condition.

We have obtained limited product liability insurance coverage for our clinical trials on humans; however, our insurance coverage may be insufficient to protect us against all product liability damages. Regardless of merit or eventual outcome, liability claims may result in decreased demand for a future product, injury to reputation, withdrawal of clinical trial volunteers, loss of revenue, costs of litigation, distraction of management and substantial monetary awards to plaintiffs. Additionally, if we are required to pay a product liability claim, we may not have sufficient financial resources to complete development or commercialization of any of our product candidates and our business and results of operations will be adversely affected. In general, insurance will not protect us against some of our own actions, such as negligence.

As our development activities progress towards the commercialization of product candidates, our liability coverage may not be adequate, and we may not be able to obtain adequate product liability insurance coverage at a reasonable cost, if at all. Even if we obtain product liability insurance, our financial position may be materially adversely affected by a product liability claim. A product liability claim could also significantly harm our reputation and delay market acceptance of our product candidates. Additionally, product recalls may be issued at the direction of the FDA, other government agencies or other companies having regulatory control for pharmaceutical sales. If a product recall occurs in the future, such a recall could adversely affect our business, financial condition or reputation.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and radioactive and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We may be unable to obtain partnerships for our product candidates, which could curtail future development and negatively affect our share price. In addition, our partners might not satisfy their contractual responsibilities or devote sufficient resources to our partnership.

Our strategy for the research, development and commercialization of our products requires entering into various arrangements with corporate collaborators, licensors, licensees and others, and our commercial success is dependent upon these outside parties performing their respective contractual responsibilities. The amount and timing of resources that such third parties will devote to these activities may not be within our control. These third parties may not perform their obligations as expected and our collaborators may not devote adequate resources to our programs. In addition, we could become involved in disputes with our collaborators, which could result in a delay or termination of the related development programs or result in litigation. We intend to seek additional collaborative arrangements to develop and commercialize some of our products. We may not be able to negotiate collaborative arrangements on favorable terms, or at all, in the future, and our current or future collaborative arrangements may not be successful.

If we cannot negotiate collaboration, license or partnering agreements, we may never achieve profitability and we may not be able to continue to develop our product candidates. Continuing Phase 1, and commencing Phase 2 and Phase 3 clinical trials for tuspentinib and luxepitinib would require significant amounts of funding and such funding may not be available to us.

### **Risks Related to Our Common Shares**

*Our share price has been and is likely to continue to be volatile and an investment in our Common Shares could suffer a decline in value.*

You should consider an investment in our Common Shares as risky and invest only if you can withstand a significant loss and wide fluctuations in the market value of your investment. The market price of our Common Shares has been highly volatile and is likely to continue to be volatile. This leads to a heightened risk of securities litigation pertaining to such volatility. Factors affecting our Common Share price include but are not limited to:

- the progress of our pre-clinical and clinical trials;
- our ability to obtain partners and collaborators to assist with the future development of our products;
- general market conditions;
- announcements of technological innovations or new product candidates by us, our collaborators or our competitors;
- published reports by securities analysts;
- developments in patent or other intellectual property rights;
- the cash and investments held by us and our ability to secure future financing;
- our ability to raise additional capital;
- public concern as to the safety and efficacy of drugs that we and our competitors develop;
- shareholder interest in our Common Shares;
- low liquidity in the daily trading volume of our Common Shares; and
- our ability to continue as a going concern.

***Future sales of our Common Shares by us or by our existing shareholders could cause our share price to fall.***

The issuance of Common Shares by us could result in significant dilution in the equity interest of existing shareholders and adversely affect the market price of our Common Shares. Sales by existing shareholders of a large number of our Common Shares in the public market and the issuance of Common Shares in connection with strategic alliances, or the perception that such additional sales could occur, could cause the market price of our Common Shares to decline and have an undesirable impact on our ability to raise capital.

***We are susceptible to stress in the global economy and therefore, our business may be affected by the current and future global financial conditions.***

If the increased level of volatility and market turmoil that have marked recent years continue, our operations, business, financial condition and the trading price of our Common Shares could be materially adversely affected. Furthermore, general economic conditions may have a great impact on us, including our ability to raise capital, our commercialization opportunities and our ability to establish and maintain arrangements with others for research, manufacturing, product development and sales.

***Failure to meet Nasdaq's continued listing requirements could result in the delisting of our Common Shares, negatively impact the price of our Common Shares and negatively impact our ability to raise additional capital.***

If we fail to satisfy the continued listing requirements of the Nasdaq Capital Market, such as the corporate governance requirements or the minimum closing bid price requirement, the exchange may take steps to delist our Common Shares. Such a delisting would likely have a negative effect on the price of our Common Shares and would impair your ability to sell or purchase our Common Shares when you wish to do so. In the event of a delisting notification, we anticipate that we would take actions to restore our compliance with applicable exchange requirements, such as stabilize our market price, improve the liquidity of our Common Shares, prevent our Common Shares from dropping below such exchange's minimum bid price requirement, or prevent future non-compliance with such exchange's listing requirements.

On July 18, 2022, we received a letter from the Nasdaq Stock Market, LLC ("Nasdaq") indicating that, for the last 30 consecutive business days, the bid price for our Common Shares had closed below the minimum \$1.00 per share required for continued inclusion on the Nasdaq Capital Market under the Nasdaq Listing Rules. The notice had no effect on the listing of our Common Shares.

Under Nasdaq Listing Rule 5810(c)(3)(A), if during the 180 calendar day period following the date of the notice the closing bid price of our Common Shares is at or above \$1.00 for a minimum of 10 consecutive business days, we would regain compliance with the minimum bid price requirement and our Common Shares would continue to be eligible for listing on the Nasdaq Capital Market, absent noncompliance with any other requirement for continued listing.

On January 18, 2023, we qualified for a 180-day extension to July 18, 2023. If we are unable to meet the minimum closing bid price requirement under Nasdaq Listing Rule 5810(c)(3)(A) by then, Nasdaq will provide notice that our securities will be subject to delisting.

We intend to monitor the closing bid price of our Common Shares and consider our available options if the closing bid price of our Common Shares remains below \$1.00 per share, including effecting a reverse stock split. There can be no assurance that we will be able to regain compliance with the minimum bid price requirement during the additional 180-day compliance period with respect to the minimum bid price requirement, or maintain compliance with the other listing requirements.

***Certain Canadian laws could delay or deter a change of control.***

Limitations on the ability to acquire and hold our Common Shares may be imposed by the *Competition Act* in Canada. This legislation permits the Commissioner of Competition of Canada to review any acquisition of a significant interest in us. This legislation grants the Commissioner jurisdiction to challenge such an acquisition before the Canadian Competition Tribunal if the Commissioner believes that it would, or would be likely to, result in a substantial lessening or prevention of competition in any market in Canada. The *Investment Canada Act* subjects an acquisition of control of a company by a non-Canadian to government review if the value of our assets, as calculated pursuant to the legislation, exceeds a threshold amount. A reviewable acquisition may not proceed unless the relevant minister is satisfied that the investment is likely to result in a net benefit to Canada. Any of the foregoing could prevent or delay a change of control and may deprive or limit strategic opportunities for our shareholders to sell their shares.

***The exercise of all or any number of outstanding stock options, the award of any additional options, restricted stock units or other stock-based awards or any issuance of shares to raise funds or acquire a business may dilute your Common Shares.***

We have in the past and may in the future grant to some or all of our directors, officers and employees options to purchase our Common Shares and other stock-based awards as non-cash incentives to those persons. The issuance of any equity securities could, and the issuance of any additional shares will, cause our existing shareholders to experience dilution of their ownership interests.

Any additional issuance of shares or a decision to acquire other businesses through the sale of equity securities may dilute our investors' interests, and investors may suffer dilution in their net book value per share depending on the price at which such securities are sold. Such issuance may cause a reduction in the proportionate ownership and voting power of all other shareholders. The dilution may result in a decline in the price of our Common Shares or a change in control.

***We do not expect to pay dividends for the foreseeable future.***

We have not paid any cash dividends to date and we do not intend to declare dividends for the foreseeable future, as we anticipate that we will reinvest future earnings, if any, in the development and growth of our business. Therefore, investors will not receive any funds unless they sell their Common Shares, and shareholders may be unable to sell their shares on favorable terms or at all. We cannot assure you of a positive return on investment or that you will not lose the entire amount of your investment in our Common Shares. Prospective investors seeking or needing dividend income or liquidity should not purchase our Common Shares.

**General Risks**

***It may be difficult for non-Canadian investors to obtain and enforce judgments against us because of our Canadian incorporation and presence.***

We are a corporation existing under the laws of Canada. Some of our directors and some of the experts named or unnamed in this Annual Report on Form 10-K, are residents of Canada, and all or a substantial portion of their assets, and a substantial portion of our assets, are located outside the United States. Consequently, although we have appointed an agent for service of process in the United States, it may be difficult for holders of our shares who reside in the United States to effect service within the United States upon our directors and officers and experts who are not residents of the United States. It may also be difficult for holders of our shares who reside in the United States to realize in the United States upon judgments of courts of the United States predicated upon our civil liability and the civil liability of our directors, officers and experts under the United States federal securities laws. Investors should not assume that Canadian courts (i) would enforce judgments of United States courts obtained in actions against us or our directors, officers or experts predicated upon the civil liability provisions of the United States federal securities laws or the securities or "blue sky" laws of any state within the United States or (ii) would enforce, in original actions, liabilities against us or our directors, officers or experts predicated upon the United States federal securities laws or any such state securities or "blue sky" laws. In addition, we have been advised by our Canadian counsel that in normal circumstances, only civil judgments and not other rights arising from United States securities legislation are enforceable in Canada and that the protections afforded by Canadian securities laws may not be available to investors in the United States.

***We are likely a “passive foreign investment company” which may have adverse United States federal income tax consequences for United States shareholders.***

United States investors in our Common Shares should be aware that we believe we are classified as a passive foreign investment company (“PFIC”) during the tax year ended December 31, 2021, and based on the nature of our business, the projected composition of our gross income and the projected composition and estimated fair market value of our assets, we expect to be a PFIC for the year ending December 31, 2022, and may be a PFIC in subsequent tax years. If the Company is a PFIC for any year during a United States shareholder’s holding period, then such United States shareholder generally will be required to treat any gain realized upon a disposition of Common Shares, or any so-called “excess distribution” received on its Common Shares, as ordinary income, and to pay an interest charge on a portion of such gain or distributions, unless the shareholder makes a timely and effective “qualified electing fund” election (“QEF election”) or a “mark-to-market” election with respect to the Common Shares. A United States shareholder who makes a QEF election generally must report on a current basis its share of the Company’s net capital gain and ordinary earnings for any year in which the Company is a PFIC, whether or not the Company distributes any amounts to its shareholders. However, United States shareholders should be aware that we do not intend to satisfy record keeping requirements that apply to a qualified electing fund, and we do not intend to supply United States shareholders with information that such United States shareholders require to report under the QEF election rules, in the event that we are a PFIC and a United States shareholder wishes to make a QEF election. Thus, United States shareholders should assume that they will not be able to make a QEF election with respect to their Common Shares. A United States shareholder who makes the mark-to-market election generally must include as ordinary income each year the excess of the fair market value of the Common Shares over the taxpayer’s basis therein. Each United States shareholder should consult its own tax advisor regarding the United States federal, United States local, and foreign tax consequences of the PFIC rules and the acquisition, ownership, and disposition of our Common Shares.

***Any failure to maintain an effective system of internal controls may result in material misstatements of our consolidated financial statements or cause us to fail to meet our reporting obligations or fail to prevent fraud; and in that case, our shareholders could lose confidence in our financial reporting, which would harm our business and could negatively impact the price of our Common Shares.***

Section 404(a) of the Sarbanes-Oxley Act of 2002 requires that our management assess and report annually on the effectiveness of our internal control over financial reporting and identify any material weaknesses in our internal control over financial reporting.

Effective internal controls are necessary for us to provide reliable financial reports and prevent fraud. If we fail to maintain an effective system of internal controls, we might not be able to report our financial results accurately or prevent fraud; and in that case, our shareholders could lose confidence in our financial reporting, which would harm our business and could negatively impact the price of our Common Shares. While we believe that we have sufficient personnel and review procedures to allow us to maintain an effective system of internal controls, we cannot assure you that we will not experience potential material weaknesses in our internal control. Even if we conclude that our internal control over financial reporting provides reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with US GAAP, because of its inherent limitations, internal control over financial reporting may not prevent or detect fraud or misstatements. Failure to implement required new or improved controls, or difficulties encountered in their implementation, could harm our results of operations or cause us to fail to meet our future reporting obligations.

If we fail to timely achieve and maintain the adequacy of our internal control over financial reporting, we may not be able to produce reliable financial reports or help prevent fraud. Our failure to achieve and maintain effective internal control over financial reporting could prevent us from complying with our reporting obligations on a timely basis, which could result in the loss of investor confidence in the reliability of our consolidated financial statements, harm our business and negatively impact the trading price of our Common Shares.

***Data security incidents and privacy breaches could result in important remediation costs, increased cyber security costs, litigation and reputational harm.***

Cyber security incidents can result from deliberate attacks or unintentional events. Cyber-attacks and security breaches could include unauthorized attempts to access, disable, improperly modify or degrade the Company's information, systems and networks, the introduction of computer viruses and other malicious codes and fraudulent "phishing" emails that seek to misappropriate data and information or install malware onto users' computers. Cyber-attacks in particular vary in technique and sources, are persistent, frequently change and are increasingly more targeted and difficult to detect and prevent against. Our network security and data recovery measures and those of third parties with which we contract, may not be adequate to protect against cyber-attacks.

Disruptions due to cyber security incidents could adversely affect our business. In particular, a cyber security incident could result in the loss or corruption of data from our research and development activities, including clinical trials, which may cause significant delays to some or all of our clinical programs. Also, our trade secrets, including unpatented know how, technology and other proprietary information could be disclosed to competitors further to a breach, which would harm our business and competitive position. We expect that risks and exposures related to cyber security attacks will remain high for the foreseeable future due to the rapidly evolving nature and sophistication of these threats. While we have invested in the protection of data and information technology, there can be no assurance that our efforts to implement adequate security measures would be sufficient to protect us against cyber-attacks.

***We must successfully upgrade and maintain our information technology systems.***

We rely on various information technology systems to manage our operations. There are inherent costs and risks associated with maintaining, modifying and/or changing these systems and implementing new systems, including potential disruption of our internal control structure, substantial capital expenditures, additional administration and operating expenses, retention of sufficiently skilled personnel to implement and operate its systems, demands on management time and other risks and costs of delays or difficulties in transitioning to new systems or of integrating new systems into our current systems. In addition, our information technology system implementations may not result in productivity improvements at a level that outweighs the costs of implementation, or at all. The implementation of new information technology systems may also cause disruptions in our business operations and have an adverse effect on our business, prospects, financial condition and operating results.

**ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

**ITEM 2. PROPERTIES**

We lease 7,556 square feet of office space in San Diego, California and 2,078 square feet of office space in Toronto, Canada. The lease for the San Diego office space was scheduled to expire on March 31, 2023. On November 4, 2022, this lease was extended through May 31, 2026, with a possible extension for an additional three years. Aptose previously leased 2,618 square feet of laboratory space in San Diego. We exited this laboratory space prior to the expiration of the lease on February 28, 2023. The costs of exit and disposition were not material. The lease for the Toronto office space was scheduled to expire on June 30, 2023. This lease was extended for one year on February 23, 2023, with this extension expiring June 30, 2024. We believe that our facilities are sufficient to meet our needs and that suitable additional space will be available as and when needed.

**ITEM 3. LEGAL PROCEEDINGS**

We know of no material pending legal proceedings to which our company or subsidiaries is a party or of which any of our properties, or the properties of our subsidiaries, is the subject. However, from time to time, we may be subject to various pending or threatened legal actions and proceedings, including those that arise in the ordinary course of our business. Such matters are subject to many uncertainties and to outcomes that are not predictable with assurance and that may not be known for extended periods of time.

**ITEM 4. MINE SAFETY DISCLOSURES**

None.



## PART II.

### ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our Common Shares are currently traded on The Nasdaq Capital Market under the symbol "APTO" and the Toronto Stock Exchange under the symbol "APS".

As of March 22, 2023, there were approximately 38 shareholders of record of our Common Shares, which included Cede & Co., a nominee for Depository Trust Company, or DTC, and CDS & Co., a nominee for The Canadian Depository for Securities Ltd., or CDS. Common shares that are held by financial institutions as nominees for beneficial owners are deposited into participant accounts at either DTC or CDS, and are considered to be held of record by Cede & Co. or CDS & Co., each as one shareholder.

We currently intend to retain all future earnings, if any, for the operation and expansion of our business and, therefore, do not anticipate declaring or paying cash dividends on our Common Shares in the foreseeable future.

#### *Repurchases of Equity Securities*

There were no repurchases of equity securities during the fourth quarter of 2022.

### ITEM 6. RESERVED

## ITEM 7 - MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*This discussion contains forward-looking statements that involve risks and uncertainties. When reviewing the discussion below, you should keep in mind the substantial risks and uncertainties that impact our business. In particular, we encourage you to review the risks and uncertainties described in "Risk Factors" in Part I, Item 1A in this Annual Report on Form 10-K. These risks and uncertainties could cause actual results to differ materially from those projected or implied by our forward-looking statements contained in this report. These forward-looking statements are made as of the date of this management's discussion and analysis, and we do not intend, and do not assume any obligation, to update these forward-looking statements, except as required by law. All amounts are expressed in United States dollars unless otherwise stated.*

Aptose Biosciences Inc. ("Aptose," the "Company," "we," "us," or "our") is a science-driven clinical stage biotechnology company committed to precision medicines addressing the unmet clinical 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's executive offices are located in San Diego, California, and our head office is located in Toronto, Canada.

### **Aptose Programs**

Aptose is advancing oral targeted agents to treat life-threatening cancers that, in most cases, are not elective for patients and require immediate treatment. We have two clinical-stage investigational products under active development for the treatment of hematologic malignancies: tuspetinib (HM43239), an oral, potent myeloid kinase inhibitor, and luxetpinib (CG-806), an oral, dual lymphoid and myeloid kinase inhibitor.

Tuspetinib is an orally administered, highly potent myeloid kinase inhibitor that selectively targets a constellation of kinases operative in myeloid malignancies and known to be involved in tumor proliferation, resistance to therapy, and differentiation. This small molecule anticancer agent is currently being evaluated in an international Phase 1/2 clinical trial in patients with relapsed or refractory AML, including the emerging populations resistant to FLT3 inhibitors.

Luxetpinib is an orally administered, highly potent dual lymphoid and myeloid kinase inhibitor that selectively targets defined clusters of kinases that are operative in hematologic malignancies. This small molecule anticancer agent is currently being evaluated in a Phase 1a/b study for the treatment of patients having B-cell malignancies including classic CLL, SLL and certain NHL that are resistant/refractory/intolerant to other therapies, and in a Phase 1 a/b study for the treatment of patients with R/R AML and HR MDS.

### **PROGRAM UPDATES**

#### ***Tuspetinib***

##### Indication and Clinical Trials:

Tuspetinib is an oral, highly potent, small molecule inhibitor of kinases operative in myeloid malignancies and known to be involved in tumor proliferation, resistance to therapy and differentiation. Preclinical *in vitro* and *in vivo* studies suggest that Tuspetinib may be an effective monotherapy and combination therapy in patients with hematologic malignancies including AML. An international Phase 1/2 clinical trial in patients with relapsed or refractory AML is ongoing. The dose escalation portion of this study to date has observed evidence of robust clinical activity, including multiple complete responses in R/R AML patients with various disease genotypes, and no toxicity trends that should prevent further dose escalation.

The FDA granted orphan drug designation to Tuspetinib for the treatment of patients with AML in October 2018. Orphan drug designation is granted by the FDA to encourage companies to develop therapies for the treatment of diseases that affect fewer than 200,000 individuals in the United States. Orphan drug status provides research and development tax credits, an opportunity to obtain grant funding, exemption from FDA application fees and other benefits. The orphan drug designation also provides us with seven additional years of marketing exclusivity in this indication.

#### Manufacturing:

Following the Tuspetinib licensing agreement between Aptose and Hanmi on November 4, 2021, Aptose received from Hanmi an existing inventory of drug product expected to support continuation of the current Phase 1/2 study. The Company and Hanmi also entered into a separate supply agreement in 2022 for additional production of new drug substance (API) and drug product to support further clinical development. Additional batches of API and drug product have been produced by other companies during 2022.

#### Program Updates at Recent Scientific Forums:

As of January 30, 2023, Aptose announced dosing of patients in the APTIVATE Phase 1/2 clinical trial of tuspetinib, and that another clinical response has been achieved by a R/R AML patient receiving 40 mg tuspetinib once daily orally in the original dose exploration trial, the second response at the recently launched low-dose 40 mg cohort. In addition, Aptose elucidated a rationale for the superior safety profile of tuspetinib. While several kinase inhibitors require high exposures that exert near complete suppression of a single target to elicit responses, those agents often cause additional toxicity because they also cause extensive inhibition of that target in normal cells. In contrast, tuspetinib simultaneously suppresses a small suite of kinase-driven pathways critical for leukemogenesis. Consequently, tuspetinib achieves clinical responses at lower exposures with less overall suppression of each pathway, thereby avoiding many of the toxicities observed with competing agents.

Tuspetinib has completed the dose escalation and dose exploration phases of an international Phase 1/2 study in patients with relapsed or refractory AML across clinical centers in the United States and South Korea. Clinical data from tuspetinib in AML were presented at the American Society of Hematology (ASH) Annual Meeting in December 2022 and presented during a Corporate Comprehensive Clinical Update Call held December 11, 2022. Data presented demonstrated that tuspetinib delivers single agent responses without prolonged myelosuppression or life-threatening toxicities in these very ill and heavily pretreated relapsed or refractory AML patients. Responses were observed in a broad range of mutationally-defined populations, including those with mutated forms of NPM1, MLL, TP53, NRAS, KRAS, DNMT3A, RUNX1, wild-type FLT3, ITD or TKD mutated FLT3, various splicing factors, and other genes. As of October 6, 2022, 60 heavily pretreated R/R 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. Tuspetinib delivered multiple complete responses (CR) at 40 mg, 80 mg, 120 mg and 160 mg dose levels in which no dose limiting toxicities ("DLT") were observed. Tuspetinib demonstrated clinically meaningful benefit in all responders, by either bridging successfully to hematopoietic stem cell transplant (HSCT) or leading to a durable response, as well as a favorable safety profile. In addition to 5 CRc and 1 PR reported at ASH 2021, 4 new CRc and 3 new PR had been generated 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 ranging from 19% to 75% were achieved in specific genotypic subpopulations of r/r AML patients. 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. 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, AE of QT prolongation or DLT were observed through the 160 mg level. Tuspetinib avoids many of the typical toxicities observed with other tyrosine kinase inhibitors. Aptose identified a safe therapeutic range with a broad therapeutic window, spanning the dose levels of 40, 80, 120 and 160 milligrams. Aptose also announced that enrollment had been initiated in the APTIVATE expansion trial for monotherapy and drug combination therapy with tuspetinib. For the APTIVATE expansion trial, Aptose selected 120 mg as the initiating single agent expansion dose and 80 mg as the initiating dose selected for combination with venetoclax.

At the European Hematology Association Annual Congress 2022 held June 9-12, 2022, Aptose presented preclinical data from tuspetinib in a poster entitled “Myeloid Kinome Inhibitor HM43239 Overcomes Acquired Resistance in Acute Myeloid Leukemia Models.” Oral HM43239 potently inhibits kinases that drive AML, including SYK, diverse forms of the FLT3, JAK1 and JAK2, and mutant forms of the c-KIT kinases. The SYK and JAK1/2 intracellular kinases and the FLT3 (mutated and wildtype) and cKIT (mutated) receptor kinases mediate oncogenic signaling pathways in AML that can drive malignant proliferation and promote drug resistance to certain drugs. Tuspetinib was developed to overcome shortcomings of other drugs, such as simple SYK inhibitors and approved inhibitors of FLT3. These preclinical findings support the continued clinical development of tuspetinib for the treatment of multiple AML populations, particularly those that who have been failed by other therapies.

Major conclusions include

- HM43239 inhibits wild type and mutant forms of FLT3 at low nM concentrations
- HM43239 inhibits SYK, JAK1, JAK2 and mutant forms of c-KIT at low nM concentrations
- HM43239 inhibits phospho-FLT3, phospho-SYK, phospho-EKRI/2 and phospho-JAK/STAT5 that participate in signaling and rescue pathways
- HM43239 has potential to kill cells and tumors resistant to other FLT3 inhibitors
- HM43239, at doses that are well tolerated, demonstrates *in vivo* efficacy on tumors resistant to other FLT3 inhibitors

### ***Luxeptinib***

#### Indication and Clinical Trials:

Luxeptinib is currently being evaluated in a Phase 1 a/b trial in patients with relapsed or refractory B cell malignancies who have failed or are intolerant to standard therapies, and in a separate Phase 1 a/b trial in patients with relapsed or refractory AML or high-risk MDS. During 2022, a new G3 formulation was tested as a single dose in 20 patients during the ongoing Phase 1 a/b clinical program. Modeling of the pharmacokinetic (PK) properties of G3 predicted 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 a significant improvement in bioavailability with G3. On November 14, 2022, Aptose announced dosing of the first AML patient to receive a continuous dosing regimen of the G3 formulation (50 mg G3 Q12h), with the protocol allowing for further dose escalation of G3 in subsequent patients. Clinical data from both studies were presented during a Corporate Comprehensive Clinical Update Call held December 11, 2022. During the Corporate Update Call, Aptose announced 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. Aptose expects that 9-15 patients will determine if G3 is safe and achieves desired exposures to deliver clinical responses.

#### Manufacturing:

During fiscal years 2017 and 2018, we created a scalable chemical synthetic route for the manufacture of luxeptinib drug substance and have scaled the manufacture of API to multi-kg levels, we completed the manufacture of a multi-kg batch of API under GMP conditions as our API supply for our first-in-human clinical trials, and we manufactured under GMP conditions two dosage strengths of capsules to serve as our clinical supply in those human studies. During fiscal 2019 and 2020, we completed successful manufacture of multiple batches of API and drug product, and planned numerous GMP production campaigns to supply the ongoing trial and planned trials into the future. To date we have been able to manufacture API and capsules to support clinical supplies under GMP conditions. In fiscal 2021 and 2022 we continued our manufacturing campaigns and scale-up and tech transfer activities to support additional manufacturing capacity for the ongoing and planned clinical trials of luxeptinib. Additional research and development funds were utilized to support the development of the G3 formulation of luxeptinib. Now that the G3 formulation has been successfully manufactured and has demonstrated encouraging PK properties, the manufacture of additional batches of the first (“G1”) and second generation formulation of luxeptinib are discontinued, and the amount of drug substance manufacturing is reduced.

#### Publication of Peer-Reviewed Research Articles Related to Luxeptinib:

During the first quarter of 2023, Aptose and its scientific collaborators published a peer reviewed research article, entitled “Luxeptinib interferes with LYN-mediated activation of SYK and modulates BCR signaling in lymphoma,” in the online journal PLOS ONE. The article elucidates the mechanism by which luxeptinib suppresses the B-cell receptor and compares it to BTK inhibitor ibrutinib. Results showed that both luxeptinib and ibrutinib are potent inhibitors of recombinant forms of BTK but have different efficacy profiles and effects on BTK activity. Luxeptinib 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 IB has little or no effect.

During the first quarter of 2022, three separate peer-reviewed research articles were published that presented preclinical data related to the application of luxeptinib to the treatment of AML, certain B-cell lymphomas and inflammation. These publications contribute to the body of preclinical data demonstrating luxeptinib’s activity as a lymphoid and myeloid kinome inhibitor, and now as an inflammation kinome inhibitor, and support its continued clinical development in several therapeutic areas.

#### Program Updates at Recent Scientific Forums:

On December 11, 2021, we presented clinical updates from luxeptinib in patients with R/R B-cell malignancies and R/R AML in two virtual poster presentations at the 63rd ASH Annual Meeting (A Phase 1 a/b Dose Escalation Study of the Mutation Agnostic BTK/FLT3 Inhibitor Luxeptinib (CG-806) in Patients with Relapsed or Refractory B-Cell Malignancies; A Phase 1 a/b Dose Escalation Study of the Mutation Agnostic FLT3/BTK Inhibitor Luxeptinib (CG-806) in Patients with Relapsed or Refractory Acute Myeloid Leukemia. The presentations highlighted that in both of these Phase 1/2 studies luxeptinib has been generally well tolerated at dose levels of 450, 600 and 750 mg BID over multiple cycles, and that patients already were being dosed at the 900 mg level. Target engagement of BTK and FLT3, and anti-tumor activity, including dose- and exposure-dependent tumor reductions, have been observed in multiple patients collectively between the studies, including in patients with follicular lymphoma, diffuse large B-cell lymphoma, CLL/SLL, and AML.

We have completed several non-clinical and clinical studies that demonstrate the highly differentiated profile of luxeptinib. Key studies that have been presented at scientific forums are as follows:

- On April 27, 2020, we presented the early clinical data on luxeptinib at the AACR Virtual Annual Meeting I in lieu of the live oral presentation originally planned. A video summary of Abstract # 9967 - *Early clinical findings from a Phase 1a/b dose escalation trial to evaluate the safety and tolerability of CG-806 in patients with relapsed or refractory CLL/SLL or non-Hodgkin’s lymphomas* described the first-in-human tests of luxeptinib which are being carried out in a Phase 1a/b clinical study in patients with significant unmet needs including patients with relapsed or refractory CLL, SLL or NHL who had been failed by or been intolerant to two lines of established therapy. We noted that the second patient, treated at the 300 mg BID dose level, represented a classic CLL patient that developed a brisk lymphocytosis (evidence of BTK target engagement and evidence of pharmacologic activity), and that enrollment was continuing.
- On June 12, 2020, we presented new clinical data on luxeptinib in a poster presentation at the 25th Congress of the EHA. The poster, *Early Clinical Findings from a Phase 1 a/b Dose Escalation Trial to Evaluate the Safety and Tolerability of CG-806 in Patients with Relapsed or Refractory CLL/SLL or Non-Hodgkin’s Lymphomas* (EHA2020 Abstract# EP711), reviewed luxeptinib data for eight patients (as of the data cut-off date on May 5, 2020) with relapsed or refractory CLL, SLL or NHL in the first in-human Phase 1a/b, open-label, single arm, multicenter dose-escalation clinical study. Data from the ongoing trial demonstrated that luxeptinib was well-tolerated in patients treated at 150 mg, 300 mg, 450 mg BID over multiple cycles, with no dose-limiting toxicities or serious adverse events observed, supporting continued dose escalation. Luxeptinib treatment achieved human steady state PK levels known to be effective in murine tumor models and led to complete inhibition of phospho-BTK and multiple CLL survival pathways. Luxeptinib treatment also led to lymphocytosis in both classic CLL patients entering study with elevated lymphocyte counts and led to complete inhibition of phospho-FLT3, suggesting that dose levels evaluated in this study may be therapeutic in patients with AML.

•On December 6, 2020, we presented new clinical data in a virtual poster presentation at the 62<sup>nd</sup> ASH Annual Meeting. The poster, *A Phase 1 a/b Dose Escalation Study of the Mutation Agnostic BTK/FLT3 Inhibitor CG-806 in Patients with Relapsed or Refractory CLL/SLL or Non-Hodgkin's Lymphomas* reviewed luxetpinib data for fourteen patients (as of the cutoff date of November 2, 2020) with relapsed or refractory CLL, SLL or NHL in the first in-human Phase 1a/b, open-label, single arm, multicenter dose-escalation clinical study. Data from the ongoing trial demonstrated that luxetpinib was generally well-tolerated in patients treated at 150 mg, 300 mg, 450 mg, and 600 mg BID over multiple cycles, supporting continued dose escalation. At the ongoing 750 mg dose, luxetpinib achieved steady state plasma concentration greater than 2 micromolar at the of Cycle 1. Luxetpinib treatment also led to modest reductions in patients with different B-cell malignancies. On December 6, 2020, Aptose also hosted a corporate event and clinical update, where the company's management highlighted some early clinical observations on safety, tolerability, pharmacokinetics and activity from the Phase 1a/b study in B-cell malignancies as well as from the recently initiated Phase 1a/b study in AML. On June 11, 2021, we presented clinical data on luxetpinib in a poster presentation at the EHA June 2021 Congress. With luxetpinib in heavily pretreated B-cell cancer patients we presented that many of the patients rapidly progressed immediately before luxetpinib treatment was initiated, resulting in a trend of tumor growth early in treatment, often followed by tumor reductions. We observed dose-dependent anti-leukemic activity to luxetpinib in patients who received dose escalation, including one follicular lymphoma patient who experienced tumor growth while on 450mg BID and upon dose escalation to 600mg BID the patient experienced 43% tumor reduction from peak (12% from baseline). In that patient, luxetpinib was well-tolerated with single agent activity for the duration of 16+ cycles of therapy. In addition, one CLL patient and one WM patient reported >25% tumor volume reduction.

•Also, on June 11, 2021, during a virtual corporate update event we provided updated clinical findings with luxetpinib for the treatment of patients with relapsed or refractory AML. We presented dose-dependent inhibition of phospho-FLT3, -BTK, -SYK, and -PDGFR $\alpha$  signaling and that all three R/R-AML patients with FLT3-ITD mutations who received 450mg BID luxetpinib (the lowest dose) for 28 days experienced blast reductions. Two patients experienced blast reduction of 67-90% but later experienced disease progression. However, one patient who failed chemotherapy twice, failed prior FLT3 inhibitor therapy, failed venetoclax and decitabine treatment and failed AHSC transplants twice, achieved a MRD-negative CR with monotherapy of 450mg BID luxetpinib.

•On December 11, 2021, we presented clinical updates from luxetpinib in patients with relapsed or refractory B-cell malignancies and relapsed or refractory AML in two virtual poster presentations at the 63<sup>rd</sup> ASH Annual Meeting (*A Phase 1 a/b Dose Escalation Study of the Mutation Agnostic BTK/FLT3 Inhibitor Luxetpinib (CG-806) in Patients with Relapsed or Refractory B-Cell Malignancies*; *A Phase 1 a/b Dose Escalation Study of the Mutation Agnostic FLT3/BTK Inhibitor Luxetpinib (CG-806) in Patients with Relapsed or Refractory Acute Myeloid Leukemia*). The presentations highlighted that in both of these Phase 1/2 studies luxetpinib has been generally well tolerated at dose levels of 450, 600 and 750 mg BID over multiple cycles, and is currently being dosed in 900 mg BID cohorts in parallel. Target engagement of BTK and FLT3, and anti-tumor activity, including dose- and exposure-dependent tumor reductions, have been observed in multiple patients collectively between the studies, including in patients with FL, DLBCL, CLL/SLL, and AML.

#### **Other corporate matters**

##### Nasdaq notice

On July 18, 2022, we received a deficiency letter (the "Deficiency Letter") from the Nasdaq Listing Qualifications Department (the "Staff") of The Nasdaq Stock Market LLC ("Nasdaq") notifying us that, for the preceding 30 consecutive business days, the closing bid price for our Common Shares was below the minimum \$1.00 per share required for continued listing on The Nasdaq Capital Market pursuant to Nasdaq Listing Rule 5550(a)(2) (the "Minimum Bid Price Requirement"). The Deficiency Letter had no immediate effect on the listing of the Company's Common Shares, and our Common Shares will continue to trade on The Nasdaq Capital Market under the symbol "APTO" at this time. Our Common Shares continue to trade on the Toronto Stock Exchange ("TSX") under the symbol "APS." Our listing on the TSX is independent and will not be affected by the Nasdaq listing status. In accordance with Nasdaq Listing Rule 5810(c)(3)(A), we were given 180 calendar days, to regain compliance with the

Minimum Bid Price Requirement. On January 18, 2023, we qualified for a 180-day extension to July 18, 2023. If we are unable to meet the minimum closing bid price requirement under Nasdaq Listing Rule 5810(c)(3)(A) by then, Nasdaq will provide notice that our securities will be subject to delisting.

We intend to monitor the closing bid price of our Common Shares and consider our available options if the closing bid price of our Common Shares remains below \$1.00 per share, including effecting a reverse stock split. There can be no assurance that we will be able to regain compliance with the minimum bid price requirement during the additional 180-day compliance period with respect to the minimum bid price requirement, or maintain compliance with the other listing requirements.

## LIQUIDITY AND CAPITAL RESOURCES

We are an early stage development company and we currently do not earn any revenues from our drug candidates. The continuation of our research and development activities and the commercialization of the targeted therapeutic products are dependent upon our ability to successfully finance and complete our research and development programs through a combination of equity financing and payments from strategic partners. We have no current sources of significant payments from strategic partners.

### *Sources of liquidity:*

The following table presents our cash and cash equivalents, investments and working capital as of December 31, 2022 and 2021.

<i>(in thousands)</i>	<b>Balances at December 31,</b>		<b>Balances at December 31,</b>	
	<b>2022</b>		<b>2021</b>	
Cash and cash equivalents	\$	36,970	\$	39,114
Investments		9,989		40,014
<b>Total</b>	<b>\$</b>	<b>46,959</b>	<b>\$</b>	<b>79,128</b>
Working capital	\$	37,235	\$	73,563

Working capital is a non-GAAP measure and represents cash, cash equivalents, investments, prepaid expenses and other current assets less current liabilities.

Management recognizes that in order for us to meet our capital requirements, and continue to operate, additional financing will be necessary. We plan to raise additional funds in order to fund our business operations. We will seek access to financing but there is no assurance that such additional funds will be available for us to finance our operations on acceptable terms, if at all. These conditions raise substantial doubt about the Company's ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. Our ability to raise additional funds could be affected by adverse market conditions, the status of our product pipeline, possible delays in enrollment in our trial, and various other factors and we may be unable to raise capital when needed, or on terms favorable to us. If necessary funds are not available, we may have to delay, reduce the scope of, or eliminate some of our development programs, potentially delaying the time to market for any of our product candidates.

Our cash needs for the next twelve months include estimates of the number of patients and rate of enrollment of our clinical trials, the amount of drug product that we will require to support our clinical trials, and our general corporate overhead costs to support our operations, and our reliance on our manufacturers. We have based these estimates on assumptions and plans which may change and which could impact the magnitude and/or timing of operating expenses and our cash runway.

Since our inception, we have financed our operations and technology acquisitions primarily from equity financing, proceeds from the exercise of warrants and stock options, and interest income on funds held for future investment.

### 2022 Base Shelf

In October 2022, we filed a short form base shelf prospectus (the 2022 “Base Shelf”) that allows us to distribute, upon the filing of prospectus supplements, up to \$200,000,000 of Common Shares, warrants, or units comprising any combination of Common Shares and warrants. The Base Shelf was declared effective by the SEC on October 21, 2022 and expires on October 7, 2025.

### At-The-Market Facilities

On December 9, 2022, the Company entered into an “at-the-market” equity distribution agreement with Jones Trading acting as the agents, the (the “2022 ATM Facility”). Under the terms of the 2022 ATM Facility, the Company may, from time to time, sell Common Shares having an aggregate offering value of up to \$50 million through Jones Trading on the Nasdaq Capital Market. During the year ended December 31, 2022, the Company issued 72,541 shares under the facility at an average price of \$0.72 for gross proceeds of \$52 thousand (\$51 thousand net of share issuance costs). Costs associated with the proceeds consisted of 3% cash commission.

On May 5, 2020, the Company entered an “at-the-market” equity distribution agreement with Piper Sandler & Co. (“Piper Sandler”) and Canaccord Genuity LLC (“Canaccord Genuity”) acting as co-agents (the “2020 ATM Facility”). Under the terms of the 2020 ATM Facility, the Company could, from time to time, sell Common Shares having an aggregate offering value of up to \$75 million through Piper Sandler and Canaccord Genuity on the Nasdaq Capital Market. During the year ended December 31, 2022, the Company issued 54,687 shares under the 2020 ATM Facility at an average price of \$0.95 for gross proceeds of \$52 thousand (\$50 thousand net of share issue costs). Costs associated with the proceeds consisted of a 3% cash commission. During the year ended December 31, 2021, the Company issued 15,315 shares under the ATM Facility at an average price of \$2.446 for gross proceeds of \$37 thousand (\$36 thousand net of share issue costs). As of October 31, 2022, the date the Agreement was terminated, the Company had raised a total of \$89 thousand gross proceeds (\$86 thousand net of share issuance costs) under the ATM Facility. Costs associated with the proceeds consisted of a 3% cash commission.

Our ability to raise additional funds could be affected by adverse market conditions, the status of our product pipeline, possible delays in enrollment in our trial related to COVID-19, and various other factors and we may be unable to raise capital when needed, or on terms favorable to us. If the necessary funds are not available, we may need to delay, reduce the scope of, or eliminate some of our development programs, potentially delaying the time to market for any of our product candidates.

### Cash flows:

The following table presents a summary of our cash flows for the years ended December 31, 2022 and 2021:

(in thousands)	For the Years Ended,	
	December 31, 2022	December 31, 2021
Net cash provided by (used in):		
Operating activities	\$ (32,322 )	\$ (43,304 )
Investing activities	30,066	(35,208 )
Financing activities	116	226
Effect of exchange rates changes on cash and cash equivalents	(4 )	7
Net (decrease)/increase in cash and cash equivalents	<u>\$ (2,144 )</u>	<u>\$ (78,279 )</u>



Cash used in operating activities:

Our cash used in operating activities for the years ended December 31, 2022 and 2021 was approximately \$32.3 million and \$43.3 million, respectively. Our uses of cash for operating activities for both years consisted primarily of salaries and wages for our employees, facility and facility-related costs for our offices and laboratories, fees paid in connection with preclinical and clinical studies, drug manufacturing costs, laboratory supplies and materials, and professional fees. In the year ended December 31, 2021, our use of cash from operating activities also included \$5.0 million in license fees paid to Hanmi for global development rights of compound tuspetinib. Net cash used in operating activities was lower in the year ended December 31, 2022 as compared with the year ended December 31, 2021 resulting mostly from lower operating expenses, as discussed further below. See “Results of Operations.”

We do not expect to generate positive cash flow from operations for the foreseeable future due to additional research and development costs, including costs related to drug discovery, preclinical testing, clinical trials, and manufacturing, as well as operating expenses associated with supporting these activities, and potential milestone payment to our collaborators. It is expected that negative cash flow will continue until such time, if ever, that we receive regulatory approval to commercialize any of our products under development and/or royalty or milestone revenue from any such products exceeds expenses.

Cash flow from investing activities:

Our cash provided by investing activities for the year ended December 31, 2022 was \$30.1 million, consisting mainly of proceeds from the maturity of investments.

Our cash used in investing activities for the year ended December 31, 2021 was \$35.2 million, and consisted of net purchases of investments of approximately \$35.0 million and purchases of property and equipment of approximately \$212 thousand.

The composition and mix of cash, cash equivalents and investments is based on our evaluation of conditions in financial markets and our near-term liquidity needs. We have exposure to credit risk, liquidity risk and market risk related to our investments. The Company manages credit risk associated with its cash and cash equivalents and investments by maintaining minimum standards of R1-low or A-low investments. The Company invests only in highly rated corporations and treasury bills which are capable of prompt liquidation. The Company manages its liquidity risk by continuously monitoring forecasts and actual cash flows. The Company is subject to interest rate risk on its cash and cash equivalents and investments. The Company does not believe that the results of operations or cash flows would be affected to any significant degree by a sudden change in market interest rates relative to interest rates on the investments, owing to the relative short-term nature of the investments.

Cash flow from financing activities:

Our cash flow from financing activities for the year ended December 31, 2022 was approximately \$116 thousand, and consisted of proceeds from the from shares issued from the 2022 ATM Facility of approximately \$51 thousand, proceeds from shares issued from the 2020 ATM Facility of \$50 thousand, and proceeds from the exercise of stock options of \$15 thousand.

Our cash flow from financing activities for the year ended December 31, 2021 was approximately \$226 thousand, and consisted mostly of proceeds from the exercise of stock options of \$190 thousand and proceeds from shares issued from the 2020 ATM Facility of approximately \$36 thousand as described above.

***Contractual Obligations and Off-Balance Sheet Financing***

As of December 31, 2022, we have not entered into any off-balance sheet arrangements.

The Company enters into research, development and license agreements in the ordinary course of business where the Company receives research services and rights to proprietary technologies. Milestone and royalty payments that may become due under various agreements are dependent on, among other factors, clinical trials, regulatory approvals and ultimately the successful development of a new drug, the outcome and timing of which is uncertain.

On November 4, 2021, the Company entered into an exclusive license agreement with Hanmi for global rights to its compound named tuspetinib. Under the Company's license agreement with Hanmi, the Company has maximum obligations for clinical development and global regulatory milestones totaling \$64.5 million for the first potential clinical indication of tuspetinib, \$34 million for the second indication, and \$29 million for the third indication. The Company has maximum obligations for tiered global sales based milestones totaling \$280 million. The Company also has an obligation for tiered royalty payments on global sales of commercialized product. The timing of any milestone or royalty payments that may become due is not yet determinable.

Under the license agreement with CG with regards to the Rights (other than the China Rights), the Company has obligations for development milestones of \$16 million related to the initiation of Phase 2 and pivotal clinical trials, and regulatory milestones totaling \$44 million. The Company also has an obligation to pay royalty payments on sales of commercialized product. The timing of any milestone or royalty payments that may become due is not yet determinable.

Under the license agreement with CG with regards to the China Rights, we entered into a license agreement with CG to gain an exclusive license to luxetpinib in China (including the People's Republic of China, Hong Kong and Macau). The Company has future obligations of development milestones of \$6 million related to approval of an IND and to the initiation of Phase 2 and pivotal clinical trials, and regulatory milestones totaling \$20 million. The Company also has an obligation to pay sales milestones and royalty payments on sales of commercialized product. The timing of any milestone or royalty payments that may become due is not yet determinable.

## RESULTS OF OPERATIONS

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

(in thousands except per Common Share data)	Year ended December 31,	
	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 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:

- 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 Phase 1 clinical trials for our product candidates tuspetinib and luxetpinib. Tuspetinib was licensed into Aptose in November 2021 and we have 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 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:

(in thousands)	Year ended December 31,	
	2022	2021
License fee – Tuspetinib	—	12,500
Program costs – Tuspetinib	10,083	57
Program costs – Luxetpinib	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
	\$ 28,088	\$ 45,985

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 luxetpinib decreased by approximately \$10.1 million, primarily due to lower manufacturing costs as a result of the current formulation requiring 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:

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

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, 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.

## CRITICAL ACCOUNTING POLICIES

### *Critical Accounting Policies and Estimates*

We periodically review our financial reporting and disclosure practices and accounting policies to ensure that they provide accurate and transparent information relative to the current economic and business environment. As part of this process, we have reviewed our selection, application and communication of critical accounting policies and financial disclosures. Management has discussed the development and selection of the critical accounting policies with the Audit Committee of the Board, and the Audit Committee has reviewed the disclosure relating to critical accounting policies in this MD&A.

### *Significant accounting judgments and estimates*

Management's assessment of our ability to continue as a going concern involves making a judgment, at a particular point in time, about inherently uncertain future outcomes and events or conditions. Please see the "Liquidity and Capital Resources" section in this document for a discussion of the factors considered by management in arriving at its assessment.

Other important accounting policies and estimates made by management are the estimates related to prepaid and accrued R&D activities, the valuation of contingent liabilities, the valuation of tax accounts, and the assumptions used in determining the valuation of share-based compensation.

### *Research and Development Activities:*

R&D costs are expensed as incurred. R&D costs consist primarily of salaries and benefits, stock-based compensation, manufacturing, contract services, clinical trials, and research related overhead. Non-refundable advance payments for goods and services that will be used in future research are recorded in prepaid and other assets and are expensed when the services are performed.

The Company records expenses for research and development activities based on Management's estimates of services received and efforts expended pursuant to contracts with vendors that conduct research and development on the Company's behalf. The financial terms vary from contract to contract and may result in uneven payment flows as compared with services performed or products delivered. As a result, the Company is required to estimate research and development expenses incurred during the period, which impacts the amount of accrued expenses and prepaid balances related to such costs as of each balance sheet date. Management estimates the amount of work completed through discussions with internal personnel and the contract research and contract manufacturing organizations as to the progress or stage of completion of the services. The Company's estimates are based on a number of factors, including the Company's knowledge of the status of each of the research and development project milestones, and contract terms together with related executed change orders. Management makes significant judgments and estimates in determining the accrued balance at the end of each reporting period.

Although Management does not expect our estimates to be materially different from amounts actually incurred, if the estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in the Company reporting amounts that are too high or too low in any particular period. As of December 31, 2022, the Company has recorded approximately \$1.3 million in prepaid expenses and approximately \$3.3 million in accrued liabilities related to its research and development activities. If the estimates are too high or too low by a factor of 10% this would mean that prepaid expenses would be over or understated by approximately \$130 thousand, and accrued liabilities would be over or understated by approximately \$330 thousand. On a combined basis, this could mean an increase or decrease in research and development expenses by approximately \$460 thousand. To date, there have been no material differences between the estimates of such expenses and the amounts actually incurred.

***Valuation of contingent liabilities:***

The Company utilizes considerable judgment in the measurement and recognition of provisions and the Company's exposure to contingent liabilities. Judgment is required to assess and determine the likelihood that any potential or pending litigation or any and all potential claims against the Company may be successful. The Company must estimate if an obligation is probable, as well as quantify the possible economic cost of any claim or contingent liability. Such judgments and assumptions are inherently uncertain. The increase or decrease of one of these assumptions could materially increase or decrease the fair value of the liability and the associated expense.

***Valuation of tax accounts:***

Uncertainties exist with respect to the interpretation of complex tax regulations and the amount and timing of future taxable income. Currently, the Company has deductible temporary differences which would create a deferred tax asset. Deferred tax assets are recognized for all deductible temporary differences to the extent that it is probable that future taxable profit will be available against which the deductible temporary differences can be utilized. Management judgment is required to determine the amount of deferred tax assets that can be recognized, based upon the likely timing and the level of future taxable profits together with future tax planning strategies. To date, the Company has determined that none of its deferred tax assets should be recognized. The Company's deferred tax assets are mainly comprised of its net operating losses from prior years and prior year research and development expenses not yet deducted for income tax purposes. These tax pools relate to entities that have a history of losses, have varying expiry dates, and may not be used to offset taxable income. As well, there are no taxable temporary differences or any tax planning opportunities available that could partly support the recognition of these losses as deferred tax assets. The generation of future taxable income could result in the recognition of some portion or all of the remaining benefits, which could result in an improvement in the Company's results of operations through the recovery of future income taxes.

***Valuation of share-based compensation:***

Management measures the costs for share based payments using market-based option valuation techniques. Assumptions are made and judgment is used in applying valuation techniques. These assumptions and judgments include estimating the future volatility of the share price, expected dividend yield, and expected life of the options. The Company uses historical data to estimate the expected dividend yield and expected volatility of its Common Shares in determining the fair value of stock options. The expected life of the options represents the estimated length of time the options are expected to remain outstanding. Such judgments and assumptions are inherently uncertain. The increase or decrease of one of these assumptions could materially increase or decrease the fair value of share- based payments and share purchase warrants issued and the associated expense.

The weighted average assumptions that were used in the Black-Scholes option pricing model to determine the fair value of stock options granted during the periods ended December 31, 2022 and 2021, respectively, are presented in Note 12 to the consolidated financial statements.

***Updated share information***

As of March 21, 2023, we had 93,005,278 Common Shares issued and outstanding. In addition, there were 19,506,857 Common Shares issuable upon the exercise of outstanding stock options.

**ITEM 7A. QUALITATIVE AND QUANTITATIVE DISCLOSURES ABOUT MARKET RISK**

Under SEC rules and regulations, as a smaller reporting company, we are not required to provide this information.

**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

The financial statements and supplementary data required pursuant to this items are included in Item 15 of this Annual Report and are presented beginning on page F-1 of this Annual Report on Form 10-K.

**ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

None.

**ITEM 9A. CONTROLS AND PROCEDURES**

As of the end of our fiscal year ended December 31, 2022, an evaluation of the effectiveness of our “disclosure controls and procedures” (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) was carried out by our management, with the participation of our principal executive officer and principal financial officer. Based upon that evaluation, our principal executive officer and principal financial officer have concluded that as of the end of that fiscal year, our disclosure controls and procedures are effective to ensure that information required to be disclosed by us in reports that we file or submit under the Exchange Act is (i) recorded, processed, summarized and reported within the time periods specified in SEC rules and forms and (ii) accumulated and communicated to our management, including our principal executive officer and principal financial officers, to allow timely decisions regarding required disclosure.

It should be noted that while our principal executive officer and principal financial officer believe that our disclosure controls and procedures provide a reasonable level of assurance that they are effective, they do not expect that our disclosure controls and procedures or internal control over financial reporting will prevent all errors or fraud. A control system, no matter how well conceived or operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Exchange Act Rule 13a-15(f). Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our principal executive and financial officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America.

As of December 31, 2022, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (2013 Framework). Based on this assessment, our management concluded that, as of December 31, 2022, our internal control over financial reporting was effective based on those criteria. We are a “smaller reporting company” as defined in Item 10(f) (1) of Regulation S-K under the Securities Act. For as long as we continue to be a smaller reporting company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not smaller reporting companies.

#### **CHANGES IN INTERNAL CONTROL OVER FINANCIAL REPORTING**

There were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) under the 1934 Act) during our fiscal quarter ended December 31, 2022, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

#### **ITEM 9B. OTHER INFORMATION**

None.

#### **ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS**

Not applicable.

### **PART III.**

Certain information required by Part III of this Annual Report on Form 10-K is omitted from this report because we are incorporating by reference to the definitive Proxy Statement for our 2023 Annual Meeting of Shareholders, referred to as the Proxy Statement, which will be filed with the SEC within 120 days of the 2022 fiscal year-end.

#### **ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

The information required by this item is incorporated herein by reference to the information from the Proxy Statement under the sections entitled “Election of Directors,” “Nomination of Directors,” and “Corporate Governance – Board Committees” and except for the information required with respect to our executive officers, which has been included under the heading “Executive Officers” in Item 1, Part I of this Form 10-K, and is incorporated herein by reference, and except for information on our code of ethics:

We have adopted a code of ethics for directors, officers (including our principal executive officer, principal financial officer and principal accounting officer) and employees, known as the Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics is available on our website at <http://www.aptose.com> under the Corporate Governance section of our Investor Relations page. We will promptly disclose on our website (i) the nature of any amendment to the policy that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of the policy that is granted to one of these specified individuals that is required to be disclosed pursuant to SEC rules and regulations, the name of such person who is granted the waiver and the date of the waiver.

#### **ITEM 11. EXECUTIVE COMPENSATION**

The information required by this item is incorporated herein by reference to the information from the Proxy Statement under the sections entitled “Executive Compensation,” and “Director Compensation.”

#### **ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

The information required by this item is incorporated herein by reference to the information from the Proxy Statement under the sections entitled “Share Ownership of Certain Beneficial Owners, Management and Directors” and “Equity Compensation Plan Information.”

#### **ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AN DIRECTOR INDEPENDENCE**

The information required by this item is incorporated herein by reference to the information from the Proxy Statement under the sections entitled “Corporate Governance - Independence of the Board” and “Interest of Related Persons in Transactions.”

#### **ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES**

The information required by this item is incorporated herein by reference to the information from the Proxy Statement under the section entitled “Audit, Audit-Related, Tax and Other Fees” and “Pre-Approval Policies and Procedures.”



PART IV.

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) Documents filed as part of this report.

1. Financial Statements. We have filed the following documents as part of this Annual Report:

<a href="#">Report of Independent Registered Public Accounting Firm (KPMG LLP, Vaughan, Canada, Auditor Firm ID: 85)</a>	Page
<a href="#">Consolidated Statements of Financial Position</a>	F-2
<a href="#">Consolidated Statements of Loss and Comprehensive Loss</a>	F-4
<a href="#">Consolidated Statements of Changes in Shareholders' Equity</a>	F-5
<a href="#">Consolidated Statements of Cash Flows</a>	F-6
<a href="#">Notes to Consolidated Financial Statements</a>	F-7
	F-8

2. Financial Statement Schedules.

All schedules are omitted because they are not applicable or the required information is shown in the Financial Statements or notes thereto.

(b) Exhibits

Exhibit Number	Description of Document
3.1	<a href="#">Articles of Incorporation, Arrangement and Amendment (incorporated herein by reference to Exhibit 99.3 to the Company's Current Report on Form 6-K filed with the SEC on June 12, 2015)</a>
3.2	<a href="#">By-law #2 of the Company (incorporated herein by reference to Exhibit 99.2 to the Company's Current Report on Form 6-K filed with the SEC on June 12, 2015)</a>
4.1*	<a href="#">Description of Securities (incorporated by reference to Exhibit 4.1 to the Company's Annual report on Form 10-K filed with the SEC on March 22, 2022)</a>
10.1	<a href="#">Indemnification Agreement dated July 10, 2007 between Lorus Therapeutics Inc. and the Company (incorporated herein by reference to Exhibit 99.1 to the Company's Current Report on Form 6-K filed with the SEC on September 4, 2007)</a>
10.2+	<a href="#">Amended and Restated Executive Employment Agreement between the Company and Dr. William G. Rice dated August 19, 2014 (incorporated herein by reference to Exhibit 4.9A to the Company's Annual Report on Form 20-F filed with the SEC on March 4, 2015)</a>
10.3+	<a href="#">Share Option Plan as amended May 5, 2015 (incorporated herein by reference to Exhibit 99.2 to the Company's Current Report on Form 6-K filed with the SEC on June 12, 2015)</a>
10.4+	<a href="#">Stock Incentive Plan as adopted May 5, 2015 (incorporated herein by reference to Exhibit 99.1 to the Company's Current Report on Form 6-K filed with the SEC on June 12, 2015)</a>
10.5+	<a href="#">Form of Executive Employment Agreement, dated December 4, 2019, between the Company and Dr. Rafael Bejar (incorporated herein by reference to Exhibit 10.7 to the Company's Annual Report filed on Form 10-K filed with the SEC on March 10, 2020)</a>
10.6^	<a href="#">License agreement dated June 13, 2018 by and between the Company and CrystalGenomics, Inc. (incorporated herein by reference to Exhibit 1.1 to the Company's Current Report on Form 6-K filed with the SEC filed on June 22, 2018)</a>
10.7^	<a href="#">Option and License Agreement between the Company and CrystalGenomics, Inc. dated March 21, 2016 (incorporated herein by reference on Form 10-KA/3 filed with the SEC on April 22, 2019)</a>

- 10.8^ [Amendment to Option and License Agreement between the Company and CrystalGenomics, Inc., dated April 26, 2016 \(incorporated herein by reference to Exhibit 99.2 to the Company's Current Report on Form 6-K filed with the SEC on June 8, 2016\)](#)
- 10.9^ [Second Amendment to Option and License Agreement between the Company and CrystalGenomics, Inc., dated May 13, 2016 \(incorporated herein by reference to Exhibit 99.3 to the Company's Current Report on Form 6-K filed with the SEC on June 8, 2016\)](#)
- 10.10^ [Third Amendment to Option and License Agreement between the Company and CrystalGenomics, Inc., dated May 19, 2016 \(incorporated herein by reference to Exhibit 99.4 to the Company's Current Report on Form 6-K filed with the SEC on June 8, 2016\)](#)
- 10.11^ [Fourth Amendment to Option and License Agreement between the Company and CrystalGenomics, Inc., dated June 1, 2016 \(incorporated herein by reference to Exhibit 99.5 to the Company's Current Report on Form 6-K filed with the SEC on June 8, 2016\)](#)
- 10.12^ [License Agreement dated as of March 6, 2018 by and between the Company and Ohm Oncology Inc. \(incorporated herein by reference to Exhibit 99.2 on Form 6-K filed with the SEC filed on March 8, 2018\)](#)
- 10.13+ [Aptose Biosciences Inc. 2021 Employee Stock Purchase Plan \( incorporated by reference to the Definitive Proxy statement on Schedule 14A filed with the SEC on April 1, 2021\)\(File no. 1-32001\)](#)
- 10.14+ [Aptose Biosciences Inc. 2021 Employee Stock Incentive Plan \( incorporated by reference to the Definitive Proxy statement on Schedule 14A filed with the SEC on April 1, 2021\)\(File no. 1-32001\)](#)
- 10.15^ [Exclusive License Agreement, dated November 4, 2021, by and between Hanmi Pharmaceutical Co. Ltd. and Aptose Biosciences Inc. \( incorporated herein by reference to Exhibit 10.1 to the Company's Current Report filed on Form 8-K on November 4, 2021\)](#)
- 10.16 [Employment Agreement dated June 3, 2019 between Aptose Biosciences Inc. and Philippe Ledru \( incorporated herein by reference to Exhibit 10.1 to the Company's Current Report filed on Form 8-K on April 11, 2022\)](#)
- 10.17 [Employment Agreement, dated June 27, 2022, between Aptose Biosciences Inc. and Fletcher Payne \( incorporated herein by reference to Exhibit 10.1 to the Company's Current Report filed on Form 8-K on June 28, 2022\)](#)
- 10.18 [Equity Distribution Agreement, dated December 9, 2022, among Aptose Biosciences Inc. and JonesTrading Institutional Services LLC\( incorporated herein by reference to Exhibit 10.1 to the Company's Current Report filed on Form 8-K on December 12, 2022\)](#)
- 21.1\* [List of Subsidiaries](#)
- 23.1\* [Consent of Independent Registered Public Accounting Firm \(KPMG\)](#)
- 24.1\* [Powers of Attorney \(included on signature page\)](#)
- 31.1\* [Certification of Principal Executive Officer Pursuant to Rules 13a-14\(a\) and 15d-14\(a\) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.](#)
- 31.2\* [Certification of Principal Financial Officer Pursuant to Rules 13a-14\(a\) and 15d-14\(a\) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.](#)
- 32.1\* [Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.](#)
- 32.2\* [Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.](#)

101.INS**	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

+ Indicates management contract or compensatory plan.

\* Filed herewith.

Confidential treatment has been sought with respect to certain portions of this exhibit.

Confidential treatment has been granted with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

\*\* In accordance with Rule 406T of Regulation S-T, the Inline XBRL related information in Exhibit 101 to this Annual Report on Form 10-K is deemed not filed or part of a registration statement or prospectus for purposes of Sections 11 or 12 of the Securities Act, is deemed not filed for purposes of Section 18 of the Exchange Act, and otherwise is not subject to liability under these sections.

#### **ITEM 16. FORM 10-K SUMMARY**

None.

## SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Diego, State of California, on the 23rd day of March, 2023.

Aptose Biosciences Inc.  
By:

/s/ William G. Rice  
William G. Rice, Ph.D.  
President, Chief Executive Officer and Chairman of the Board of Directors

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Dr. William G. Rice and Mr. Fletcher Payne, and each of them, his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or either of them, or their or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

### Signature

### Title

/s/ William G. Rice  
William G. Rice, Ph.D.

President, Chief Executive Officer and Chairman of the Board of Directors  
(Principal Executive Officer)

/s/ Fletcher Payne  
Fletcher Payne

Senior Vice President and Chief Financial Officer (Principal Financial Officer and Accounting Officer)

/s/ Denis R. Burger  
Denis R. Burger, Ph.D.

Director, Lead Independent

/s/ Carol G. Ashe  
Carol G. Ashe

Director

/s/ Erich M. Platzer  
Erich M. Platzer, M.D., Ph.D.

Director

/s/ Bernd R. Seizinger  
Bernd R. Seizinger, M.D., Ph.D.

Director

/s/ Mark D. Vincent  
Mark D. Vincent, M.D.

Director

/s/ Warren Whitehead  
Warren Whitehead

Director



Consolidated Financial Statements

**APTOSE BIOSCIENCES INC.**

Years ended December 31, 2022 and 2021



*Aptose Biosciences Inc.*

KPMG LLP  
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Tel 905-265 5900  
Fax 905-265 6390  
www.kpmg.ca

**Report of Independent Registered Public Accounting Firm**

To the Shareholders and Board of Directors

Aptose Biosciences Inc.:

*Opinion on the Consolidated Financial Statements*

We have audited the accompanying consolidated statements of financial position of Aptose Biosciences Inc. and subsidiaries (the Company) as of December 31, 2022 and 2021, the related consolidated statements of loss and comprehensive loss, changes in shareholders' equity, and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

*Going Concern*

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Notes 1 and 2 (a) to the consolidated financial statements, the Company has suffered recurring losses from operations and has a net capital deficiency that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Notes 1 and 2 (a). The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

*Basis for Opinion*

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

KPMG LLP, an Ontario limited liability partnership and member firm of the KPMG global organization of independent member firms affiliated with KPMG International Limited, a private English company limited by guarantee. KPMG Canada provides services to KPMG LLP.



*Critical Audit Matter*

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

*Research and Development Prepaid and Accrued Costs*

As discussed in Notes 2(i), 4 and 9 to the consolidated financial statements, the Company records expenses for research and development activities based on Management's estimates of services received and efforts expended pursuant to contracts with vendors that conduct research and development on the Company's behalf. The financial terms vary from contract to contract and may result in uneven payment flows as compared with services performed or products delivered. As a result, the Company is required to estimate research and development expenses incurred during the period, which impacts the amount of accrued expenses and prepaid balances related to such costs as of each balance sheet date. Management estimates the amount of work completed through discussions with internal personnel and the contract research and contract manufacturing organizations as to the progress or stage of completion of the services. The Company's estimates are based on a number of factors, including the Company's knowledge of the status of each of the research and development project milestones, and contract terms together with related executed change orders. Management makes significant judgments and estimates in determining the accrued balance at the end of each reporting period.

We identified the evaluation of research and development prepaid and accrued costs as a critical audit matter. Higher degree of auditor judgment was required in evaluating the results of our audit procedures because of the subjectivity and estimation uncertainty associated with this estimate.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design of certain internal controls related to the critical audit matter. This included controls over the development of the estimated amount of prepaid and accrued costs incurred by the contract research and contract manufacturing organizations. For a selection of research and development projects, we assessed the Company's estimates of a selection of the research and development activities completed to date by:

- inquiring with Company personnel responsible for overseeing the research and development activities to understand progress of the activities including project milestones, and contract terms together with related executed change orders
- inspecting the terms of the contracts, including related executed change orders, between the Company and the respective contract research and contract manufacturing organizations, the correspondence between the Company and these organizations as to the completion status, and using this information to arrive at an independent estimate of the prepaid or accrual amounts and comparing it to the amounts recorded by the Company

We have served as the Company's auditor since 1994.

/s/KPMG LLP

Chartered Professional Accountants, Licensed Public Accountants  
Vaughan, Canada

March 23, 2023

**APTOSE BIOSCIENCES INC.**

Consolidated Statements of Financial Position  
(Expressed in thousands of US dollars)

	December 31, 2022	December 31, 2021
<b>Assets</b>		
<b>Current assets:</b>		
Cash and cash equivalents	\$ 36,970	\$ 39,114
Investments	9,989	40,014
Prepaid expenses	2,303	2,476
Other current assets	257	133
<b>Total current assets</b>	<b>49,519</b>	<b>81,737</b>
<b>Non-current assets:</b>		
Property and equipment	211	323
Right-of-use assets, operating leases	1,297	465
<b>Total non-current assets</b>	<b>1,508</b>	<b>788</b>
<b>Total assets</b>	<b>\$ 51,027</b>	<b>\$ 82,525</b>
<b>Liabilities and Shareholders' Equity</b>		
<b>Current liabilities:</b>		
Accounts payable	\$ 6,326	\$ 1,699
Accrued liabilities	5,657	6,016
Current portion of lease liability, operating leases	301	459
<b>Total current liabilities</b>	<b>12,284</b>	<b>8,174</b>
<b>Non-current liabilities:</b>		
Lease liability, operating leases	1,002	115
<b>Total liabilities</b>	<b>13,286</b>	<b>8,289</b>
<b>Shareholders' equity:</b>		
<b>Share capital:</b>		
Common shares, no par value, unlimited authorized shares, 92,367,275 and 92,215,024 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	437,520	437,386
Additional paid-in capital	68,869	63,673
Accumulated other comprehensive loss	(4,318)	(4,316)
<b>Deficit</b>	<b>(464,330)</b>	<b>(422,507)</b>
<b>Total shareholders' equity</b>	<b>37,741</b>	<b>74,236</b>
<b>Total liabilities and shareholders' equity</b>	<b>\$ 51,027</b>	<b>\$ 82,525</b>

See accompanying notes to consolidated financial statements.

Going concern, see Note 2.

Commitments, see Note 10.

Subsequent events, see Notes 1, 10 and 16.



**APTOSE BIOSCIENCES INC.**

## Consolidated Statements of Loss and Comprehensive Loss

(Expressed in thousands of US dollars, except for per common share data)

	Year ended December 31, 2022	Year ended December 31, 2021
Revenue	\$ —	\$ —
Expenses:		
Research and development	28,088	45,985
General and administrative	14,514	19,462
Operating expenses	42,602	65,447
Other income:		
Interest income	788	94
Foreign exchange gain/(loss)	(9 )	(1 )
Total other income	779	93
Net loss	(41,823 )	(65,354 )
Other comprehensive loss:		
Unrealized 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 )
Weighted average number of common shares outstanding used in the calculation of (in thousands)		
Basic and diluted loss per common share	<u>92,267</u>	<u>89,086</u>

See accompanying notes to consolidated financial statements.

**APTOSE BIOSCIENCES INC.**

Consolidated Statements of Changes in Shareholders' Equity  
(Expressed in thousands of US dollars, except for per common share data)

	Common Shares		Additional paid-in capital	Accumulated other comprehensive loss	Deficit	Total
	Shares (thousands)	Amount				
Balance, December 31, 2021	92,215	\$ 437,386	\$ 63,673	\$ (4,316)	\$ (422,507)	\$ 74,236
Common shares issued under the October 2022 ATM	73	51	—	—	—	51
Common shares issued under the May 2020 ATM	55	50	—	—	—	50
Common shares issued upon exercise of stock options	14	26	(11)	—	—	15
Stock-based compensation	—	—	5,207	—	—	5,207
Common shares issued under the ESPP plan	11	7	—	—	—	7
Other comprehensive loss	—	—	—	(2)	—	(2)
Net loss	—	—	—	—	(41,823)	(41,823)
Balance, December 31, 2022	<u>92,368</u>	<u>\$ 437,520</u>	<u>\$ 68,869</u>	<u>\$ (4,318)</u>	<u>\$ (464,330)</u>	<u>\$ 37,741</u>
Balance, December 31, 2020	88,882	\$ 429,523	\$ 50,861	\$ (4,316)	\$ (357,153)	\$ 118,915
Common shares issued pursuant to the Hanmi licensing fees	3,236	7,500	—	—	—	7,500
Common shares issued under the May 2020 ATM	15	36	—	—	—	36
Common shares issued upon exercise of stock options	82	327	(137)	—	—	190
Stock-based compensation	—	—	12,949	—	—	12,949
Net loss	—	—	—	—	(65,354)	(65,354)
Balance, December 31, 2021	<u>92,215</u>	<u>\$ 437,386</u>	<u>\$ 63,673</u>	<u>\$ (4,316)</u>	<u>\$ (422,507)</u>	<u>\$ 74,236</u>

See accompanying notes to consolidated financial statements.

**APTOSE BIOSCIENCES INC.**

 Consolidated Statements of Cash Flows  
 (Expressed in thousands of US dollars)

	Year ended December 31, 2022	Year ended December 31, 2021
<b>Cash flows from operating activities:</b>		
Net loss for the year	\$ (41,823 )	\$ (65,354 )
<b>Items not involving cash:</b>		
Stock-based compensation	5,207	12,949
Shares issued to Hanmi Pharmaceutical as license fees	—	7,500
Depreciation and amortization	120	150
Disposal of property and equipment	16	—
Amortization of right-of-use assets	408	472
Interest on lease liabilities	35	43
Unrealized foreign exchange gain/(loss)	4	(7 )
Accrued interest on investments	(60 )	(18 )
<b>Change in operating working capital:</b>		
Prepaid expenses	173	78
Operating lease payments	(546 )	(555 )
Other assets	(124 )	(4 )
Accounts payable	4,627	(472 )
Accrued liabilities	(359 )	1,914
Cash used in operating activities	(32,322 )	(43,304 )
<b>Cash flows from financing activities:</b>		
Issuance of common shares under 2022 ATM	51	—
Issuance of common shares under 2020 ATM	50	36
Issuance of common shares pursuant to exercise of stock options	15	190
Cash provided by financing activities	116	226
<b>Cash flows from (used in) investing activities:</b>		
Maturity (acquisition) of investments, net	30,090	(34,996 )
Purchase of property and equipment	(24 )	(212 )
Cash provided by (used in) investing activities	30,066	(35,208 )
Effect of exchange rate fluctuations on cash and cash equivalents held	(4 )	7
Decrease in cash and cash equivalents	(2,144 )	(78,279 )
Cash and cash equivalents, beginning of year	39,114	117,393
Cash and cash equivalents, end of year	<u>\$ 36,970</u>	<u>\$ 39,114</u>

See accompanying notes to consolidated financial statements.

**I. Reporting entity:**

Aptose Biosciences Inc. (“Aptose,” the “Company,” “we,” “us,” or “our”) is a science-driven clinical stage biotechnology company committed to precision medicines addressing the unmet clinical 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’s executive offices are located in San Diego, California, and our head office is located in Toronto, Canada.

We are advancing targeted agents to treat life-threatening cancers that, in most cases, are not elective for patients and require immediate treatment. We have two clinical-stage investigational products for hematological malignancies: tuspetinib, an oral, potent myeloid kinase inhibitor, and luxetpinib, an oral, dual lymphoid and myeloid kinase inhibitor.

Since our inception, we have financed our operations and technology acquisitions primarily from equity financing, proceeds from the exercise of warrants and stock options, and interest income on funds held for future investment. Our uses of cash for operating activities have primarily consisted of salaries and wages for our employees, facility and facility-related costs for our offices and laboratories, fees paid in connection with preclinical and clinical studies, drug manufacturing costs, laboratory supplies and materials, and professional fees.

Management recognizes that in order for us to meet our capital requirements, and continue to operate, additional financing will be necessary. We plan to raise additional funds in order to fund our business operations. We will seek access to financing but there is no assurance that such additional funds will be available for us to finance our operations on acceptable terms, if at all. These conditions raise substantial doubt about the Company’s ability to continue as a going concern, see Note 2(a). The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Our ability to raise additional funds could be affected by adverse market conditions, the status of our product pipeline, possible delays in enrollment in our trial, and various other factors and we may be unable to raise capital when needed, or on terms favorable to us. If necessary funds are not available, we may have to delay, reduce the scope of, or eliminate some of our development programs, potentially delaying the time to market for any of our product candidates.

We do not expect to generate positive cash flow from operations for the foreseeable future due to the early stage of our clinical trials. It is expected that negative cash flow will continue until such time, if ever, that we receive regulatory approval to commercialize any of our products under development and/or royalty or milestone revenue from any such products exceeds expenses.

Our cash needs for the next twelve months include estimates of the number of patients and rate of enrollment of our clinical trials, the amount of drug product that we will require to support our clinical trials, and our general corporate overhead costs to support our operations, and our reliance on our manufacturers. We have based these estimates on assumptions and plans which may change and which could impact the magnitude and/or timing of operating expenses and our cash runway, See Note 2(a).

The Company’s financial statements are prepared using generally accepted accounting principles in the United States of America applicable to a going concern which contemplates the realization of assets and liquidation of liabilities in the normal course of business. As of December 31, 2022, the Company has an accumulated deficit of approximately \$464.3 million; cash and cash equivalents and investment balances of approximately \$47.0 million; and working capital of approximately \$37.2 million. Management recognizes that in order for us to meet our capital requirements, and continue to operate, additional financing will be necessary. We plan to raise additional funds in order to fund our business operations through equity financing under the 2022 Base Shelf or the 2022 ATM Facility. We will seek access to financing but there is no assurance that such additional funds will be available for us to finance our operations on acceptable terms, if at all. These conditions raise substantial doubt about the Company’s ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

On July 18, 2022, we received a letter from the Nasdaq Stock Market, LLC (“Nasdaq”) indicating that, for the last 30 consecutive business days, the bid price for our Common Shares had closed below the minimum \$1.00 per share required for continued inclusion on the Nasdaq Capital Market under the Nasdaq Listing Rules. Under Nasdaq Listing Rule 5810(c)(3)(A), if during the 180 calendar day period following the date of the notice the closing bid price of our Common Shares is at or above \$1.00 for a minimum of 10 consecutive business days, we would regain compliance with the minimum bid price requirement and our Common Shares would continue to be eligible for listing on the Nasdaq Capital Market, absent noncompliance with any other requirement for continued listing.

On January 18, 2023, we qualified for a 180-day extension to July 18, 2023. If we are unable to meet the minimum closing bid price requirement under Nasdaq Listing Rule 5810(c)(3)(A) by then, Nasdaq will provide notice that our securities will be subject to delisting.

## **2. Significant accounting policies**

### **(a) Basis of presentation - Going concern**

These consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States, or GAAP and the rules and regulations of the Securities and Exchange Commission, or SEC, related to annual reports filed on Form 10-K, assuming the Company will continue as a going concern. The going concern assumption contemplates the realization of assets and satisfaction of liabilities in the normal course of business. However, substantial doubt about the Company's ability to continue as a going concern exists.

As of December 31, 2022, the Company had an accumulated deficit of approximately \$464.3 million, cash and investment balances of approximately \$47.0 million, and working capital of approximately \$37.2 million. In order for the Company to meet its capital requirements, and continue to operate, additional financing will be necessary. The Company is evaluating strategies to obtain the required additional funding for future operations. These strategies may include, but are not limited to, obtaining equity financing, and restructuring of operations to decrease expenses. However, given the impact of the economic downturn on the U.S. and global financial markets, the Company may be unable to access further equity or when needed. As such, there can be no assurance that the Company will be able to obtain additional liquidity when needed or under acceptable terms, if at all. The consolidated financial statements do not reflect any adjustments to the carrying amounts and classification of assets, liabilities, and reported expenses that may be necessary if the Company were unable to continue as a going concern. Such adjustments may be material.

The functional and presentation currency of the Company is the US dollar.

### **(b) Basis of consolidation:**

These consolidated financial statements include the accounts of its subsidiaries. All intercompany transactions, balances, revenue, and expenses are eliminated on consolidation.

### **(c) Significant accounting policies, estimates and judgments**

The preparation of the consolidated financial statements requires management to make judgments, estimates and assumptions that affect the application of accounting policies and reported amounts of assets and liabilities at the date of the consolidated financial statements and reported amounts of revenue and expenses during the reporting period. Actual outcomes could differ from those estimates. The consolidated financial statements contain estimates, which by their nature, are uncertain.

The impacts of such estimates are pervasive throughout the consolidated financial statements and may require accounting adjustments based on future occurrences.

The estimates and underlying assumptions are reviewed on a regular basis. Revisions to accounting estimates are recognized in the period in which the estimate is revised and in any future periods affected.

(d) Leases

The Company's operating leases of tangible property with terms greater than twelve months are recognized as right of use assets, which represents the lessee's right to use, or control the use of, a specified asset for the lease term, and a corresponding lease liability, which represents the lessee's obligation to make lease payments under a lease, measured on a discounted basis. Landlord inducements in the form of free rent periods are netted against lease payments to the landlord in measuring right-of-use assets and lease liabilities.

(e) Cash and cash equivalents:

Cash and cash equivalents are short-term highly liquid investments with original maturities of 90 days or less as of the date of purchase. Cash equivalents are accounted for an amortized cost basis, which approximates their fair value due to their short-term maturities.

(f) Investments:

Investments consist of term deposits with original maturities greater than 90 days and are classified by management as securities available-for-sale. These available-for-sale securities are recorded at estimated fair values. Unrealized gains and losses on these investments are recorded in accumulated other comprehensive income (AOCI) in shareholder's equity. Realized gains and losses and declines in value that are judged to be other than temporary are included in interest income.

(g) Concentration of risk:

The Company is subject to credit risk from the Company's cash and cash equivalents and investments. The carrying amount of the financial assets represents the maximum credit exposure. The Company manages credit risk associated with its cash and cash equivalents and investments by maintaining minimum standards of R1-low or A-low investments and the Company invests only in highly rated corporations and treasury bills, which are capable of prompt liquidation.

The Company has cash accounts in Canada and the US. The Canada Deposit Insurance Corporation (CDIC) and the US Federal Deposit Insurance Corporation (FDIC) provide insurance to protect depositors against the loss of their deposits in case of a bank failure. However, the maximum amount of coverage varies by jurisdiction and account type. In Canada, the CDIC insures eligible deposits up to \$100,000 (CAD) per depositor, per insured category, per member institution. In the United States, the FDIC insures deposits up to \$250,000 per depositor, per insured bank, for each account ownership category. It is important to note that not all deposits are eligible for insurance coverage. For example, deposits in foreign currency, deposits held in trust, and investments such as mutual funds, stocks, and bonds are not insured by either the FDIC or CDIC.

The Company is subject to intermediary risk associated with the actions of financial intermediaries, such as banks or investment managers, who act on behalf of clients to buy and sell assets. The Company has diversified the investments with two large financial institutions to reduce the concentration of risk in any one institution, and spread the risk. This measure reduces the likelihood of being significantly impacted by the failure of a single financial institution.

The Company has reduced the exposure to individual investment vehicles to minimize the risk of loss in case of adverse events. The Company has diversified the investment portfolio across different asset classes and investment vehicles to achieve this goal.

(h) Property and equipment:

Property and equipment is measured at cost less accumulated depreciation and accumulated impairment losses. Cost includes expenditures that are directly attributable to the acquisition of the asset. The Company records depreciation at rates that charge operations with the cost of the assets over their estimated useful lives on a straight-line basis as follows:

Office furniture	5 years
Laboratory equipment	5 years
Computer hardware	3 years
Computer software	3 years
Leasehold improvements	Life of lease

The residual value, useful life and methods of depreciation of the assets are reviewed at each reporting period and adjusted prospectively if appropriate.

(i) Research and development:

Research and development (R&D) costs are expensed as incurred. R&D costs consist primarily of salaries and benefits, stock-based compensation, manufacturing, contract services, clinical trials and research related overhead. Non-refundable advance payments for goods and services that will be used in future research are recorded in prepaid and other assets and are expensed when the services are performed.

The Company records expenses for research and development activities based on Management's estimates of services received and efforts expended pursuant to contracts with vendors that conduct research and development on the Company's behalf. The financial terms vary from contract to contract and may result in uneven payment flows as compared with services performed or products delivered. As a result, the Company is required to estimate research and development expenses incurred during the period, which impacts the amount of accrued expenses and prepaid balances related to such costs as of each balance sheet date. Management estimates the amount of work completed through discussions with internal personnel and the contract research and contract manufacturing organizations as to the progress or stage of completion of the services. The Company's estimates are based on a number of factors, including the Company's knowledge of the status of each of the research and development project milestones, and contract terms together with related executed change orders. Management makes significant judgments and estimates in determining the accrued balance at the end of each reporting period.

(j) Fair value:

The Company measures its financial assets and liabilities at fair value. The carrying amounts for the Company's financial instruments, including cash and cash equivalents, accounts payable and accrued liabilities approximate their fair value due to their short maturities. Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date.

(k) Stock-based compensation:

The Company has a stock-based compensation plan (the "Plan") available to officers, directors, employees, and consultants with grants under the Plan approved by the Company's Board of Directors. Under the Plan, the exercise price of each option equals the closing trading price of the Company's stock on the day prior to the grant if the grant is made during the trading day or the closing trading price on the day of the grant if the grant is issued after markets have closed. Vesting is provided for at the discretion of the Board of Directors and the expiration of options is to be no greater than 10 years from the date of grant.

The Company uses the fair value based method of accounting for employee awards granted under the Plan. The Company calculates the fair value of each stock option grant using the Black-Scholes option pricing model at the grant date. The stock-based compensation cost of the options is recognized as stock-based compensation expense over the relevant vesting period of the stock options using an estimate of the number of options that will eventually vest.

Stock options awarded to non-employees are measured at the grant-date fair value of the equity instruments issued in accordance with FASB accounting standards update No 2018-07, Topic 718.

The Company has a stock incentive plan pursuant to which the Board may grant equity settled stock-based awards comprised of restricted stock units or dividend equivalents to employees, officers, consultants, independent contractors, advisors and non-employee directors of the Company. Compensation cost for restricted share units is measured at fair value at the date of grant, which is the market price of the underlying security, and is expensed over the award's vesting period on a straight-line basis using an estimate of the number of awards that will eventually vest.

(l)Segment reporting:

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker, or CODM. The Company's Chief Executive Officer serves as its CODM. The Company views its operations and manages its business as one segment, which is the discovery and development of personalized therapies addressing unmet medical needs in oncology. The Company operates primarily in the US.

(m)Loss per share:

Basic loss per share is computed by dividing the net loss available to common shareholders by the weighted average number of shares outstanding during the year. Diluted loss per share is computed similarly to basic loss per share except that the weighted average share outstanding is increased to include additional shares for the assumed exercise of stock options and warrants, if dilutive. The number of additional shares is calculated by assuming that outstanding stock options and warrants were exercised and that the proceeds from such exercises were used to acquire common stock at the average market price during the year. The inclusion of the Company's stock options and warrants in the computation of diluted loss per share has an anti-dilutive effect on the loss per share and, therefore, they have been excluded from the calculation of diluted loss per share.

(n)Income taxes:

The Company accounts for income taxes under the asset and liability method. Under this method, deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted rates in effect for the year in which these temporary differences are expected to be recovered or settled. Valuation allowances are provided if, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company provides reserves for potential payments of tax to various tax authorities related to uncertain tax positions and other issues. Reserves are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filing is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. Potential interest and penalties associated with such uncertain tax positions are recorded as components of income tax expense. As of December 31, 2022 and December 31, 2021, the Company has not recorded any reserves for potential payments as the Company has a history of losses and does not have any revenue from operations.

(o) Recent Accounting Pronouncements

There were various accounting standards and interpretations issued recently, none of which are expected to have a material impact on our financial position, operations, or cash flows.

**3. Cash and cash equivalents:**

Cash and cash equivalents consists of cash of \$596 thousand (December 31, 2021 - \$294 thousand), deposits in high interest savings accounts, money market funds and accounts with original maturities less than 90 days totaling \$36.374 million (December 31, 2021 - \$38.820 million). See Note 16, Subsequent Events.



**4. Prepaid expenses:**

	December 31, 2022		December 31, 2021	
Prepaid research and development expenses	\$	1,271	\$	632
Prepaid insurance		893		1,811
Other prepaid expenses		139		33
Total	\$	<u>2,303</u>	\$	<u>2,476</u>

**5. Property and equipment:**

December 31, 2022	Cost	Accumulated depreciation	Net book value
Laboratory equipment	\$ 197	\$ 48	\$ 149
Computer hardware	198	177	21
Computer software	222	222	—
Office furniture	140	117	23
Leasehold improvements	184	166	18
Total	<u>\$ 941</u>	<u>\$ 730</u>	<u>\$ 211</u>

December 31, 2021	Cost	Accumulated depreciation	Net book value
Laboratory equipment	\$ 369	\$ 188	\$ 181
Computer hardware	198	144	54
Computer software	222	222	—
Office furniture	140	95	45
Leasehold improvements	184	141	43
Total	<u>\$ 1,113</u>	<u>\$ 790</u>	<u>\$ 323</u>

In the year ended December 31, 2022, the company recorded a loss on disposition of fixed assets of \$16 thousand, with these assets having had an original cost of \$196 thousand and accumulated depreciation of \$180 thousand. Also in the year ended December 31, 2022, the Company had additions to fixed assets of \$24 thousand.

**6. Right-of-use assets, operating leases:**

	Year ended December 31, 2022		Year ended December 31, 2021	
Right-of-use assets, beginning of year	\$	1,860	\$	1,848
Additions to right-of-use assets		1,240		12
Right-of-use assets, end of year		3,100		1,860
Accumulated amortization		(1,803)		(1,395)
Right-of use assets, NBV	\$	<u>1,297</u>	\$	<u>465</u>

**7. Investments:**

Investments consisted of the following as of December 31, 2022 and December 31, 2021:

	Cost	December 31, 2022 Unrealized gain		Market value
United States Treasury Bills	\$ 9,991	\$	(2)	\$ 9,989
Total	<u>\$ 9,991</u>	<u>\$</u>	<u>(2)</u>	<u>\$ 9,989</u>

	Cost	December 31, 2021	
		Unrealized gain	Market value
Guaranteed Investment Certificate	\$ 20,016	\$ —	\$ 20,016
Commercial notes	19,998	—	19,998
<b>Total</b>	<b>\$ 40,014</b>	<b>\$ —</b>	<b>\$ 40,014</b>

The short-term U.S. Treasury Bills recorded as investments as of December 31, 2022 had maturities of one year.

**8. Fair value measurements and financial instruments:**

The fair value hierarchy establishes three levels to classify the inputs to valuation techniques used to measure fair value.

Level 1 - inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities;

Level 2 - inputs are quoted prices in markets that are not active, quoted prices for similar assets or liabilities in active markets, inputs other than quoted prices that are observable for the asset or liability, or inputs that are derived principally from or corroborated by observable market data or other means; and

Level 3 - inputs are unobservable (supported by little or no market activity).

The fair value hierarchy gives the highest priority to Level 1 inputs and the lowest priority to Level 3 inputs.

The following table presents the fair value of the Company's financial instruments for the periods presented:

	December 31, 2022	Level 1	Level 2	Level 3
<b>Assets</b>				
Money Market accounts	\$ 165	\$ —	\$ 165	\$ —
Money Market Funds	22,343	—	22,343	—
High interest savings accounts	13,866	—	13,866	—
United States Treasury Bills	9,989	—	9,989	—
<b>Total</b>	<b>\$ 46,363</b>	<b>\$ —</b>	<b>\$ 46,363</b>	<b>\$ —</b>

	December 31, 2021	Level 1	Level 2	Level 3
<b>Assets</b>				
Money Market accounts	\$ 17,974	\$ —	\$ 17,974	\$ —
Money Market Funds	15,801	—	15,801	—
High interest savings accounts	5,045	—	5,045	—
Commercial notes	19,998	—	19,998	—
Guaranteed Investment Certificate	20,016	—	20,016	—
<b>Total</b>	<b>\$ 78,834</b>	<b>\$ —</b>	<b>\$ 78,834</b>	<b>\$ —</b>

**9. Accrued liabilities:**

Accrued liabilities as of December 31, 2022 and December 31, 2021 consisted of the following:

	December 31, 2022	December 31, 2021
Accrued personnel-related costs	\$ 2,302	\$ 2,152
Accrued research and development expenses	3,122	3,520
Other accrued expenses	233	344
<b>Total</b>	<b>\$ 5,657</b>	<b>\$ 6,016</b>

**10. Lease liability**

Aptose leases office space in San Diego, California and Toronto, Canada. The lease for the San Diego office space was scheduled to expire on March 31, 2023. On November 4, 2022, this lease was extended through May 31, 2026 (the "Third Amendment"). Management has determined that the Third Amendment represents a lease modification, as defined by ASC 842, *Leases*, does not meet the requirements for accounting as a separate contract and continues to meet the definition of an operating lease. Accordingly, the Company has accounted for the Third Amendment prospectively, via remeasurements, on the Modification Date, to the lease liability and corresponding right-of-use asset. Aptose previously leased lab space in San Diego, which we exited prior to the expiration of the lease on February 28, 2023. The costs incurred in exiting this laboratory space were not material. We lease office space in Toronto, Ontario, Canada, with this lease previously scheduled to expire on June 30, 2023. This lease was extended for one year on February 23, 2023, with this extension expiring on June 30, 2024. The Company has not included any extension periods in calculating its right-to-use assets and lease liabilities. The Company also enters into leases for small office equipment.

Minimum payments, undiscounted, under our operating leases are as follows:

Years ending December 31,	
2023	\$ 394
2024	447
Thereafter	659
Total	<u>\$ 1,500</u>

To calculate the lease liability, the lease payments in the table above were discounted over the remaining term of the leases using the Company's incremental borrowing rate as of January 1, 2019 for existing leases at the time of adopting ASC 842, and for new leases after the date adoption, as of the date of the execution date of the new lease. The following table presents the weighted average remaining term of the leases and the weighted average discount rate:

	December 31, 2022	December 31, 2021
Weighted-average remaining term – operating leases (years)	3.3	1.2
Weighted-average discount rate – operating leases	6.62 %	5.37 %
Lease liability, current portion	\$ 301	\$ 459
Lease liability, long term portion	1,002	115
Lease liability, total	<u>\$ 1,303</u>	<u>\$ 574</u>

Operating lease costs and operating cash flows from our operating leases are as follows:

	Year ended December 31, 2022	Year ended December 31, 2021
Operating lease cost	\$ 443	\$ 515
Operating cash flows from operating leases	\$ 546	\$ 555

**11. Share capital:**

The Company has authorized share capital of an unlimited number of common voting shares.

(a) Equity issuances:

(i) 2022 At-The-Market ("ATM") Facility

On December 9, 2022, the Company entered into an equity distribution agreement with Jones Trading acting as the agent in connection with the 2022 ATM Facility. Under the terms of the 2022 ATM Facility, the Company may, from time to time, sell Common Shares having an aggregate offering value of up to \$50 million through Jones Trading on the Nasdaq Capital Market. During the year ended December 31, 2022, the Company issued 72,541 shares under this ATM Facility at an average price of \$0.72 for gross proceeds of \$52 thousand (\$51 thousand net of share issuance costs). Costs associated with the proceeds consisted of 3% cash commission.

(ii) Hanmi Licensing Payment

On December 9, 2021, the Effective date, the Company entered into an exclusive license agreement with Hanmi Pharmaceutical Co. Ltd. (Hanmi) for global rights to tuspetinib. Pursuant to the terms of this agreement, on December 14, 2021, the Company issued 3,235,548 Common Shares as a partial upfront payment to Hanmi in consideration of the license and other rights granted for a total cost of \$7.5 million. The number of Common Shares issued is determined using the average market closing price of the Common Shares on the Nasdaq stock market over the five (5) trading day period ending on the Effective Date. See also Note 13, Collaborative agreements.

(iii) 2020 At-The-Market ("ATM") Facility

On May 5, 2020, the Company entered into an equity distribution agreement with Piper Sandler and Canaccord Genuity (the "Agreement") acting as co-agents in connection with the 2020 ATM Facility. Under the terms of the 2020 ATM Facility, the Company may, from time to time, sell Common Shares having an aggregate offering value of up to \$75 million through Piper Sandler and Canaccord Genuity on the Nasdaq Capital Market. During the period from January 1, 2022 to October 21, 2022, the date the Agreement was terminated, the Company issued 54,687 shares under this ATM equity facility at an average price of \$0.95 for gross proceeds of \$52 thousand (\$50 thousand net of share issuance costs). During the year ended December 31, 2021, the Company issued 15,315 shares under the facility at an average price of \$2.446 for gross proceeds of \$37 thousand (\$36 thousand net of share issue costs). As of October 21, 2022, the date the Agreement was terminated, the Company had raised a total of \$89 thousand gross proceeds (\$86 thousand net of share issuance costs) under the 2020 ATM Facility. Costs associated with the proceeds consisted of a 3% cash commission.

(b) Loss per share:

Loss per common share is calculated using the weighted average number of Common Shares outstanding and is presented in the table below:

(in thousands)	Year ended December 31, 2022	Year ended December 31, 2021
Net loss	\$ (41,823 )	\$ (65,354 )
Weighted-average common shares – basic and diluted	92,267	89,086
Net loss per share – basic and diluted	<u>\$ (0.45 )</u>	<u>\$ (0.73 )</u>

The effect of any potential exercise of the Company's stock options outstanding during the years ended December 31, 2022 and December 31, 2021 has been excluded from the calculation of diluted loss per common share as it would be anti-dilutive.

**12. Stock-based compensation:**

(a) Stock option plan and employee stock purchase plan

Effective June 1, 2021, the Company adopted a new stock incentive plan (New Incentive Plan) and an employee stock purchase plan (ESPP).

The New Incentive Plan authorizes the Board of Directors to administer the New Incentive Plan to provide equity-based compensation in the form of stock options, stock appreciation rights, restricted stock, restricted stock units and Dividend Equivalents.

The Corporation currently maintains its existing Share Option Plan and 2015 Stock Incentive Plan (2015 SIP). Effective June 1, 2021 no further grants will be made under the Share Option Plan or 2015 SIP, though existing grants under the Share Option Plan will remain in effect in accordance with their terms.

The aggregate number of our common shares, no par value, that may be issued under all awards under the New Incentive Plan is (i) 6,343,242, plus (ii) any of our Common Shares subject to any outstanding award under our prior plans that, after June 1, 2021, are not purchased or are forfeited or reacquired by us, or otherwise not delivered to the participant due to termination, cancellation or cash settlement of such award subject to the share counting provisions of the New Incentive Plan.

Under both the Share Option Plan and the New Incentive Plan, the exercise price of each option equals the closing trading price of the Company's stock on the day prior to the grant if the grant is made during the trading day or the closing trading price on the day of grant if the grant is issued after markets have closed. Vesting is provided for at the discretion of the Board of Directors and the expiration of options is to be no greater than 10 years from the date of grant.

The Company uses the fair value-based method of accounting for employee awards granted under both plans. The Company calculates the fair value of each stock option grant using the Black-Scholes option pricing model at the grant date. The stock-based compensation cost of the options is recognized as stock-based compensation expense over the relevant vesting period of the stock options using an estimate of the number of options that will eventually vest.

The ESPP, which is administered by the Board of Directors, allows eligible employees of the Company with an opportunity to purchase Common Shares through accumulated payroll deductions up to a maximum 15% of eligible compensation. The ESPP will be implemented by consecutive offering periods with a new offering period commencing on the first trading day on or after February 1 and August 1 each year, or on such other date as the Board of Directors will determine, and continuing thereafter until terminated in accordance with the Plan. Unless the Board of Directors provides otherwise, the purchase price will be equal to eighty-five percent (85%) of the fair market value of a Common Share on the offering date or the exercise date, whichever is lower.

The maximum number of Common Shares which will be made available for sale under the ESPP will be 1,700,000 Common Shares.

The first six-month offering period began on February 1, 2022 and ended on August 1, 2022. There were 10,858 Common Shares issued under the ESPP as of December 31, 2022 (December 31, 2021 - nil). The second six-month period began on August 1, 2022 and ended on February 1, 2023.

Stock option transactions for the year ended December 31, 2022 and December 31, 2021, are summarized as follows:

	Options (in thousands)	Weighted average exercise price	Weighted average remaining contractual life (years)	Aggregate Intrinsic Value
Outstanding, December 31, 2020	11,942	\$ 4.97		
Granted	4,659	3.84		
Exercised	(82)	2.32		
Forfeited	(1,407)	5.38		
Outstanding, December 31, 2021	15,112	\$ 4.61		
Granted	6,295	1.19		
Exercised	(14)	1.08		
Forfeited	(4,890)	3.84		
Outstanding, December 31, 2022	16,503	\$ 3.48	6.8	\$ —
Exercisable, December 31, 2022	8,251	\$ 4.52	5.4	\$ —
Vested and expected to vest, December 31, 2022	15,263	\$ 3.57	6.7	\$ —

Aggregate intrinsic value represents the excess of the value of the closing stock price on the previous trading day of the respective balance sheet dates over the exercise price of the stock options. Total intrinsic value of options exercised was \$3 thousand for 2022 (2021 – \$222 thousand).

As of December 31, 2022, there was \$2.68 million of total unrecognized compensation cost related to non-vested stock options, which is expected to be recognized over an estimated weighted-average period of 1.52 years.

The following table presents the weighted average assumptions that were used in the Black-Scholes option pricing model to determine the fair value of stock options granted during the period, and the resultant weighted average fair values:

	Year ended December 31, 2022	Year ended December 31, 2021
Risk-free interest rate	2.17 %	0.59 %
Expected dividend yield	—	—
Expected volatility	82.7 %	81.8 %
Expected life of options (years)	5	5
Grant date fair value	\$ 0.79	\$ 2.47

The Company uses historical data to estimate the expected dividend yield and expected volatility of its Common Shares in determining the fair value of stock options. The expected life of the options represents the estimated length of time the options are expected to remain outstanding.

The following table presents the vesting terms of options granted in the period:

	Year ended December 31, 2022 Options (in thousands)	Year ended December 31, 2021 Options (in thousands)
Cliff vesting after one year anniversary	—	—
3-year vesting (50%-25%-25%)	425	430
4-year vesting (50%-16 2/3%-16 2/3%-16 2/3%)	5,270	3,429
Earlier of performance criteria or 4 years	600	800
Total stock options granted in the year	6,295	4,659

During the year ended December 31, 2022, the option agreements of one Company officer were modified as part of a separation and release agreement. Vested options of 851,053, with exercise prices ranging from \$1.34 to \$6.91, were allowed to continue to be exercisable for an additional 12-month period, and also 477,166 options that would have expired unvested, were allowed to continue to vest for a 12-month period. As there was no service requirement, during the year ended December 31, 2022, the company recorded \$67 thousand in additional compensation related to these modifications.

During the year ended December 31, 2022, the Company issued 600,000 performance stock options (PSOs) to one officer of the Company. 500,000 PSOs will vest in tranches connected with financing events, and the remaining 100,000 PSOs will vest in connection with licensing and partnering events. If any performance triggers are not attained, such unvested PSOs will vest on the fourth anniversary of the grant.

During the year ended December 31, 2021, the option agreements of one officer were modified as part of a separation and release agreement. Vested options of 1,679,169, with exercise prices ranging from \$1.03 to \$7.44, were allowed to continue to be exercisable for an additional 12-month period, and also 504,833 options that would have expired unvested were allowed to continue to vest for a 12-month period. As there was no service requirement, during the year ended December 31, 2021, the Company recorded \$945 thousand and \$663 thousand additional compensation related to these modifications for the vested and unvested options, respectively. All options expired on December 31, 2022.

During the year ended December 31, 2021, the Company issued 800,000 performance stock option (PSO) to two officers of the Company. One officer received 400,000 PSOs, of which 200,000 PSOs will vest in tranches connected with financing events, and the remaining 200,000 PSOs will vest in connection with licensing and partnering events. The other officer received 400,000 PSOs, of which 200,000 PSOs will vest in tranches connected to dose escalation trials and the remaining 200,000 PSOs will vest in connection with expansion trials. If such performance triggers are not attained, such PSOs will vest on the fourth anniversary of the grant. On November 11, 2021, the performance criteria connected with the financing events were met, and 200,000 PSOs were vested.

(b)Share-based payment expense

The Company recorded share-based payment expense related to stock options and RSUs as follows:

	Year ended December 31, 2022	Year ended December 31, 2021
Research and development	\$ 2,218	\$ 3,789
General and administrative	2,989	9,160
Total	\$ 5,207	\$ 12,949

**13. Collaborative agreements:**

The Company enters into research, development and license agreements in the ordinary course of business where the Company receives research services and rights to proprietary technologies. Milestone and royalty payments that may become due under various agreements are dependent on, among other factors, clinical trials, regulatory approvals and ultimately the successful development of a new drug, the outcome and timing of which is uncertain.

On November 4, 2021, the Effective Date, the Company entered into an exclusive license agreement with Hanmi Pharmaceutical Co. Ltd. (Hanmi) for global rights to its compound named tuspetinib. In consideration of the license and other rights granted, Aptose made an upfront payment to Hanmi in the amount of \$12.5 million, including \$5.0 million in cash and \$7.5 million in Aptose Common Shares (the “Shares”). The number of Shares issued was determined using the average market closing price of the Common Shares on the NASDAQ stock market over the five (5) trading day period ending on the Effective Date. Accordingly, Aptose issued 3,235,548 shares to Hanmi.

Under the Company’s license agreement with Hanmi, the Company has maximum obligations for clinical development and global regulatory milestones totaling \$64.5 million for the first potential clinical indication of tuspetinib, \$34 million for the second indication, and \$29 million for the third indication. The company has maximum obligations for tiered global sales-based milestones totaling \$280 million. The Company also has an obligation for tiered royalty payments on global sales of commercialized product. The timing of any milestone or royalty payments that may become due is not yet determinable.

Under the Company’s license agreement with CrystalGenomics for rights to luxepitinib, in all territories outside of the Republic of Korea and China, the Company has obligations for development milestones of \$16 million related to the initiation of Phase 2 and pivotal clinical trials, and regulatory milestones totaling \$44 million. The Company also has an obligation to pay royalty payments on sales of commercialized product. The timing of any milestone or royalty payments that may become due is not yet determinable.

On June 13, 2018, the Company entered into a license agreement with CrystalGenomics to gain an exclusive license to luxepitinib in China. The Company has potential future obligations of development milestones of \$6 million related to approval of an Investigational New Drug (“IND”) and to the initiation of Phase 2 and pivotal clinical trials, and regulatory milestones totaling \$20 million. The Company also has an obligation to pay sales milestones and royalty payments on sales of commercialized product. The timing or likelihood of any milestone or royalty payments that may become due is not yet determinable.

**14. Income taxes:**

(a) Income taxes

For the years ended December 31, 2022 and 2021, the total comprehensive loss is as follows:

	December 31, 2022	December 31, 2021
Loss attributed to US foreign operations	\$ (36,615 )	\$ (52,447 )
Loss attributed to Canadian operations	(5,208 )	(12,907 )
Loss before income taxes	<u>\$ (41,823 )</u>	<u>\$ (65,354 )</u>



(b) Tax rate reconciliation

Major items causing the Company's income tax rate to differ from the statutory rate of approximately 26.5% (December 31, 2021 – 26.5%) are as follows:

	Year ended December 31, 2022	Year ended December 31, 2021
Net loss	\$ (41,823 )	\$ (65,354 )
Statutory Canadian corporate tax rate	26.5 %	26.5 %
Computed expected tax recovery	\$ (11,083 )	\$ (17,319 )
Non-deductible permanent differences	1,376	3,707
Change in valuation allowance	10,821	15,274
Foreign tax rate differential	(466 )	(683 )
Prior year true-up adjustments	(703 )	(951 )
Other	55	(28 )
	<u>\$ —</u>	<u>\$ —</u>

(c) Significant components of deferred taxes

The tax effects of temporary differences that give rise to significant portions of the unrecognized deferred tax assets are presented below:

	December 31, 2022	December 31, 2021
Net operating losses carried forward	\$ 60,092	\$ 49,286
Research and development expenditures	5,023	5,032
Property, equipment, and other intangible assets	7,264	7,261
Research and development tax credits	4,968	4,202
Financing costs	873	1,580
Right-of-use assets	2	40
Total deferred tax assets	78,222	67,401
Valuation allowance	(78,222 )	(67,401 )
Net deferred tax asset	\$ —	\$ —

The valuation allowance at December 31, 2022 was primarily related to net operating loss carryforwards that, in the judgment of management, are not more-likely than-not to be realized. In assessing the realizability of deferred tax assets, management considers whether it is more-likely-than-not that all or some portion of the deferred assets will not be realized. This ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the period in which those deductible temporary difference become deductible. Based on the history of losses and projections for future taxable income, management believes that it is not more-likely than-not that the Company will realize the benefits of these deductible temporary differences (e.g. deferred tax assets).

The Company has certain deductible Canadian research and development expenditures that have not been deducted for tax purposes, totaling \$19.0 million, that can be carried forward indefinitely. The Company also has Canadian non-refundable federal and provincial investment tax credits of approximately \$3.0 million which are available to reduce future federal taxes payable and begin to expire in 2023, as well as non-refundable US research and development tax credits of approximately \$2.6 million which are available to reduce future US taxes payable and begin to expire in 2038.

In addition, the Company has Canadian non-capital loss carryforwards of \$216.9 million. To the extent that the non-capital loss carryforwards are not used, they begin to expire in 2026. The Company also has a US non-capital loss carryforward of \$1.0 million. To the extent that the non-capital loss carryforwards are not used, they begin to expire in 2034.

The Company files income tax returns with Canada and its provinces and territories. Generally, we are subject to routine examinations by the Canada Revenue Agency ("CRA"). Income tax returns filed with various provincial jurisdictions are generally open to examination for periods of four to five years subsequent to the filing of the respective return.

The Company also files income tax returns for our U.S. operations and subsidiary with the U.S. federal and state tax jurisdictions. Generally, we are subject to routine examination by taxing authorities in the U.S. jurisdictions. There are presently no examination of our U.S. federal and U.S. state returns. We believe that our tax positions comply with the applicable tax law.

**15. Selected quarterly financial data (unaudited):**

Selected financial data (unaudited) for the periods presented was as follows:

	March 31, 2022	June 30, 2022	September 30, 2022	December 31, 2022
Revenue	\$ —	\$ —	\$ —	\$ —
Net loss	(11,481)	(10,565)	(9,777)	(10,000)
Basic and diluted loss per common share	(0.12)	(0.11)	(0.11)	(0.11)

  

	March 31, 2021	June 30, 2021	September 30, 2021	December 31, 2021
Revenue	\$ —	\$ —	\$ —	\$ —
Net loss	(16,227)	(13,470)	(11,333)	(24,324)
Basic and diluted loss per common share	(0.18)	(0.15)	(0.13)	(0.27)

**16. Subsequent events**

Subsequent to the year end, the Company issued 3,219,600 stock options to directors, officers, employees and consultants with an average exercise price of \$0.67. 2,461,400 stock options vest 50% after one year and 16.67% on each of the next three anniversaries, and 725,000 options vest 50% after one year and 25% on each of the next two anniversaries.

On January 19, 2023, the Company granted 570,000 RSUs with immediate vesting. On February 6, 2023, all of these restricted stock units were redeemed for 570,000 Common Shares.

On March 13, 2022, the Company transferred all of its cash deposits from Silicon Valley Bank to a large US bank with a strong credit rating. The Company has securities held in custody at a different large, credit-worthy US bank, in money market accounts invested in US treasury notes. The Company established direct relationships with this bank after the closure of Silicon Valley Bank.



Subsidiaries of the Registrant

Name	State/Jurisdiction of Incorporation
Aptose Biosciences U.S. Inc.	Delaware
NuChem Pharmaceuticals Inc.	Ontario, Canada

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KPMG LLP  
100 New Park Place, Suite 1400 Vaughan, ON L4K 0J3  
Tel 905-265 5900  
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www.kpmg.ca

**Consent of Independent Registered Public Accounting Firm**

The Board of Directors  
Aptose Biosciences Inc.

We consent to the incorporation by reference in the registration statement (No. 333- 267801) on Form S-3 and the registration statements (No. 333-257446, No. 333- 228794, and No. 333-205158) on Form S-8 of our report dated March 23, 2023, with respect to the consolidated financial statements of Aptose Biosciences Inc. which comprise the consolidated statements of financial position as at December 31, 2022 and December 31, 2021, the related consolidated statements of loss and comprehensive loss, changes in shareholders' equity and cash flows for each of the years then ended, and the related notes, which report appears in the December 31, 2022 annual report on Form 10-K of Aptose Biosciences Inc. for the fiscal year ended December 31, 2022

/s/ KPMG LLP

Chartered Professional Accountants, Licensed Public Accountants

March 23, 2023  
Vaughan, Canada

KPMG LLP, an Ontario limited liability partnership and member firm of the KPMG global organization of independent member firms affiliated with KPMG International Limited, a private English company limited by guarantee. KPMG Canada provides services to KPMG LLP.

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## Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, William G. Rice, certify that:

1. I have reviewed this Annual Report on Form 10-K of Aptose Biosciences Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's fourth fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2023

/s/ William G. Rice  
Name: William G. Rice, Ph.D.  
Title: President and Chief Executive Officer

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## CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Fletcher Payne, certify that:

1. I have reviewed this Annual Report on Form 10-K of Aptose Biosciences Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's fourth fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2023

/s/ Fletcher Payne  
Name: Fletcher Payne  
Title: Senior Vice President and Chief Financial Officer

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**Certification Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002**

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, I, William G. Rice, the President and Chief Executive Officer of Aptose Biosciences Inc. (the "Company"), hereby certify that, to my knowledge:

- 1.The Annual Report on Form 10-K for the year ended December 31, 2021 (the "Report") of the Company fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934; and
- 2.The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 23, 2023

/s/ William G. Rice

Name: William G. Rice, Ph.D.

Title: President and Chief Executive Officer

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**Certification Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002**

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, I, Fletcher Payne, the Senior Vice President and Chief Financial Officer of Aptose Biosciences Inc. (the "Company"), hereby certify that, to my knowledge:

1. The Annual Report on Form 10-K for the year ended December 31, 2021 (the "Report") of the Company fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 23, 2023

/s/ Fletcher Payne

Name: Fletcher Payne

Title: Senior Vice President and Chief Financial Officer

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