

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM 10-K

(Mark one)

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

For the fiscal year ended December 31, 2018.

TRANSITION REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

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)

**98-1136802**

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

**251 Consumers Road, Suite 1105  
Toronto, Ontario, Canada M2J 4R3**  
(Address of principal executive offices)

**647-479-9828**

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:  
Common Shares, without par value      The Nasdaq Stock 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 Section 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 (§229.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). YES  NO

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10 K or any amendment to this Form 10 K.

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

Large accelerated filer   
Non-accelerated filer   
Emerging growth company

Accelerated filer   
Smaller reporting company

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 registrant is a shell company (as defined in Rule 12b-2 of the 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, 2018 was \$134,370,583.00.

As of March 12, 2019, the registrant had 41,499,112 shares of common stock outstanding.

#### **DOCUMENTS INCORPORATED BY REFERENCE**

*Portions of our Proxy Statement for our 2019 Annual Meeting of Stockholders (the "Proxy Statement"), are incorporated by reference in Part III*

---

## TABLE OF CONTENTS

<u>PART I.</u>	<u>1</u>
<u>ITEM 1A. RISK FACTORS</u>	<u>17</u>
<u>ITEM 1B. UNRESOLVED STAFF COMMENTS</u>	<u>34</u>
<u>ITEM 2. PROPERTIES</u>	<u>34</u>
<u>ITEM 3. LEGAL PROCEEDINGS</u>	<u>34</u>
<u>ITEM 4. MINE SAFETY DISCLOSURES</u>	<u>34</u>
<u>PART II.</u>	<u>34</u>
<u>ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES</u>	<u>34</u>
<u>ITEM 6. SELECTED FINANCIAL DATA</u>	<u>34</u>
<u>ITEM 7 - MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS</u>	<u>35</u>
<u>ITEM 7A. QUALITATIVE AND QUANTITATIVE DISCLOSURES ABOUT MARKET RISK</u>	<u>44</u>
<u>ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA</u>	<u>44</u>
<u>ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE</u>	<u>44</u>
<u>ITEM 9A. CONTROLS AND PROCEDURES</u>	<u>44</u>
<u>ITEM 9B. OTHER INFORMATION</u>	<u>44</u>
<u>PART III.</u>	<u>45</u>
<u>ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE</u>	<u>45</u>
<u>ITEM 11. EXECUTIVE COMPENSATION</u>	<u>45</u>
<u>ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS</u>	<u>45</u>
<u>ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AN DIRECTOR INDEPENDENCE</u>	<u>45</u>
<u>ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES</u>	<u>45</u>
<u>PART IV.</u>	<u>46</u>
<u>ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES</u>	<u>46</u>
<u>ITEM 16. FORM10-K SUMMARY</u>	<u>47</u>

---

*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, 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 stock” refers to our common stock, no par value.*

*Beginning with this annual report on Form 10-K, Aptose will be filing reports with the Securities and Exchange Commission as a smaller reporting company and a domestic issuer instead of a foreign private issuer.*

*This report contains the following trademarks, trade names and service marks 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 is a science-driven biotechnology company advancing highly differentiated agents to treat unmet medical needs in life-threatening cancers, such as acute myeloid leukemia (“AML”), certain B-cell malignancies, high-risk myelodysplastic syndromes (“MDS”) and other hematologic malignancies. Aptose is a publicly listed company incorporated under the laws of Canada. The Company's shares are listed on the Nasdaq Capital Markets and the Toronto Stock Exchange. The Company was incorporated on September 5, 1986 under the name RML Medical Laboratories (“RML”) pursuant to the Business Corporations Act (Ontario). Between 1986 and 2014, the Company operated under the names of RML, IMUTEC Corporation and Lorus Therapeutics Inc. On August 28, 2014, the Company changed its name from Lorus Therapeutics Inc. to Aptose Biosciences Inc. and on October 1, 2014 we consolidated our outstanding common shares (the “Common Shares”) on the basis of one post-consolidation Common Share for each twelve pre-consolidation Common Shares.

Based on insights into the genetic and epigenetic profiles of certain cancers and patient populations, Aptose is building a pipeline of novel and targeted oncology therapies directed at dysregulated processes and signaling pathways in cancer cells, and this strategy is intended to optimize efficacy through simultaneous targeting of key drivers of disease in cancer cells, while preserving quality of life in patients by minimizing the side effects associated with conventional therapies. Our product pipeline includes cancer drug candidates that exert potent activity as stand-alone agents and that enhance the activities of other anticancer agents without causing overlapping toxicities. Indeed, we believe our targeted products can emerge as first-in-class or best-in-class agents that deliver single agent benefit and may serve as part of a combination therapeutic strategy for specific populations of cancer patients.

We believe the future of cancer treatment and management lies in the prospective selection and treatment of patients having malignancies that are genetically or epigenetically predisposed to response based on a drug's unique mechanism of action. We are of the view that many drugs currently approved for the treatment and management of cancer are not selective for the specific genetic alterations (targets) and pathways that cause the patient's tumor and hence allow for disease progression and /or significant toxicities due to off-target effects. Aptose's strategy is to develop agents that target underlying disease-promoting mutations or altered pathways within a patient population, and we intend to apply this strategy across several therapeutic indications in oncology, including hematologic malignancies and solid tumor indications.

#### **Aptose Programs**

Aptose has one clinical-stage program, one Investigational New Drug (“IND”)—stage program, and a third program that is discovery-stage and partnered with another company.

- CG-806, a investigational new drug (“IND”) application was submitted February 22, 2019 to the U.S. Food and Drug Administration (“FDA”) for CG026806 (“CG-806”), Aptose's pan-FMS-like tyrosine kinase 3 / pan-Bruton's tyrosine kinase (“pan-FLT3/pan-BTK”) inhibitor. Development of CG-806 is intended for the treatment of patients having certain B-cell malignancies [including chronic lymphocytic leukemia (“CLL”), small lymphocytic lymphoma (“SLL”) and certain non-Hodgkin's lymphomas (“NHL”) that are resistant/refractory/intolerant to other therapies], as well as for patients with relapsed/refractory Acute Myeloid Leukemia (“R/R AML”), including the emerging populations resistant to FLT3 inhibitors.

---

- APTO-253, our clinical-stage program, is a small molecule MYC inhibitor and is currently enrolling patients in a Phase 1b clinical trial for the treatment of patients with R/R blood cancers, including AML and high-risk Myelodysplastic Syndrome (hr MDS).
- APL-581, our partnered program, is a dual bromodomain and extra-terminal domain motif (BET) protein and kinase inhibitor program which we partnered to OHM Oncology on March 7, 2018.

Aptose is committed to the development of anticancer drugs that target aberrant oncologic signaling that underlies a particular life-threatening malignancy. This targeted approach is intended to impact the disease-causing events in cancer cells without affecting normal processes within cells. Such an approach requires that we first identify critical underlying oncogenic mechanisms in cancer cells and then develop a therapeutic that selectively impacts such oncogenic mechanisms.

- As a multi-kinase pan-FLT3 / pan-BTK inhibitor, CG-806 targets multiple critical pathways that overlap to lead to the proliferation of cancer cells, including the B-cell receptor signaling pathway and FLT3 receptor pathways, as well as other receptor kinases and signaling cascades that drive dysregulated survival of the cancer cells.
- Further, Aptose created the APTO-253 small molecule targeted drug that inhibits expression of the MYC oncogene and is under development as a novel therapy for AML and related MDS. Dysregulation of the MYC oncogene reprograms signaling of cancer cells to allow for malignant transformation and resistance to typical anticancer drugs. APTO-253 directly targets the MYC gene and inhibits production of MYC mRNA and protein, thereby leading to cancer cell death.

The following table sets forth various product conditions in our pipeline and their respective stages of development.

DRUG	TARGET	INDICATION	DISCOVERY	PRE-CLINICAL	PHASE 1	PHASE 2
<b>CG-806</b>	Pan-FLT3	AML	Completed			
<b>CG-806</b>	BTK-WT/C481S	B Cell Cancers (CLL/MCL/DLBCL)	Completed			
<b>APTO-253</b>	c-Myc	AML / MDS	Completed			Ongoing
<b>APL-581 (Partnered)</b>	BRD/Kinase	Hematologic Malignancies	Completed			

Completed Ongoing

## CG-806 Program

### Overview

On May 7, 2018, we exercised an option by paying \$2.0 million in cash to South Korean company CrystalGenomics, Inc. (“CG”), in order to purchase an exclusive license to research, develop and commercialize CG-806 in all countries of the world except the Republic of Korea and China, for all fields of use. CG-806 is a highly potent, orally bioavailable non-covalent small molecule being developed for AML and certain B-cell malignancies because of its actions as a pan-FLT3/pan-BTK inhibitor. Subsequently, on June 14, 2018 we announced that we entered into a license agreement with CG for Aptose to gain a license for China Rights to CG-806 (including the People’s Republic of China, Hong Kong and Macau). 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, including an issued patent in China, to CG-806, a first-in-class, highly potent oral small molecule being developed for AML, B-cell malignancies and other hematologic malignancies.

CG-806 exhibits a picomolar IC50 toward the FMS-like tyrosine kinase 3 (“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”). Consequently, CG-806 is characterized as a pan-FLT3/pan-BTK inhibitor. Further, CG-806 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, EGFR and ErbB2/4 kinases that are responsible for safety concerns with certain other kinase inhibitors.

As a potent inhibitor of FLT3-ITD, CG-806 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, CG-806 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 CG-806 targets all forms of FLT3 and several other key oncogenic pathways, and that CG-806 was well tolerated from a safety perspective during efficacy and formal Good Laboratory Practice (“GLP”) toxicology studies, suggest that CG-806 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, for patients with B cell malignancies, CG-806 may be a preferable inhibitor over alternatives such as ibrutinib or other commercially approved development stage BTK inhibitors in certain circumstances. Overexpression of the BTK enzyme can drive oncogenic signaling of certain B cell malignancies, including chronic lymphocytic leukemia (“CLL”) and certain non-Hodgkin’s lymphomas (“NHL”) such as mantle cell lymphoma (“MCL”), 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, CG-806 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 CG-806 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 CG-806 kills B cell malignancy cell lines on average approximately 1000 times more potently than ibrutinib and kills ibrutinib-resistance cancer cells, and that CG-806 more potently killed primary malignant cells taken from the bone marrow of CLL and ALL B-cell cancer patients. Yet, CG-806 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 CG-806 therapy. This is particularly true since CG-806 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.

### Role of BTK in B-cell signaling

BTK, a member of the TEC family kinase, is an essential element of B-cell receptor (“BCR”) signaling, which is required for B-cell maturation, survival and proliferation. It is an upstream activator of multiple pro-survival / anti-apoptotic pathways, including the NF-KB, mTOR-AKT and ERK pathways. BTK is overexpressed in malignant cells from patients with various B-cell malignancies, such as CLL, MCL, AML, and DLBCL. Disruption of BCR signaling via inhibition of BTK, has been shown to lead to clinical remissions in these patients.

Binding studies of CG-806 have confirmed non-covalent, reversible inhibition of BTK, FLT3-ITD and Aurora Kinase A. Ibrutinib, a commercially-approved, covalent BTK inhibitor, possesses a Michael acceptor to react with C481 in BTK and irreversibly inactivates the BTK enzyme. In contrast, CG-806 does not require reactivity with the C481 residue for inhibition of the BTK enzyme, thereby allowing CG-806 to inhibit the wild type and C481 mutant form of the BTK enzyme.

*Preclinical In Vitro Evaluation of CG-806*

CG-806 is a potent inhibitor of BTK and FLT3 wild types, as well as the BTK C481S and FLT3-ITD mutants, which represent major sources of therapy relapse or are negative prognostic signals in patients. In enzymatic assays, CG-806 has demonstrated potency against the BTK C481S mutant with a half maximal inhibitory concentration (IC50) of 2.5 nanomolar (nM). CG-806 also has potent activity against the FLT3-ITD mutation, occurring in 30-35% of AML patients, with an IC50 against the purified enzyme of 0.8nM (800pM). Likewise, CG-806 exerts low nM IC50 values against the FLT3 enzyme having various mutations in the tyrosine kinase domain (TKD) and the Gatekeeper region, and CG-806 has the ability to potently suppress the CSF1R, PDGFR $\alpha$ , AKT/mTOR/S6K, ERK, MYC and AURK/H3S10 pathways. Finally, CG-806 does not exhibit any inhibition of epidermal growth factor receptor ("EGFR"), TEC or ErbB2/4 kinases. Inhibition of one or more of these kinases has been speculated to contribute to the toxicity observed from the commercially approved BTK inhibitor.

BTK is overexpressed in the blast cells of approximately 80% of AML patients as compared to normal peripheral blood mononuclear cells ("PBMCs") in healthy subjects. Researchers have shown that BTK inhibition attenuates the proliferation and survival of FLT3-ITD primary AML blasts and AML cell lines, as well as inhibits the downstream activation of FLT3-ITD-dependent MYC and STAT5 kinases. We believe that CG-806 is the only drug in development that inhibits both FLT3-ITD and BTK pathways reported to synergize to drive the proliferation and survival of AML.

*CG-806 Xenograft Studies*

In vivo subcutaneous AML tumor models of anti-cancer efficacy revealed CG-806 induced rapid and sustained tumor eradication (Figure 1a). CG-806 was administered orally once daily, for 14 days. Moreover, CG-806 exhibited the sustained tumor elimination post therapy, while demonstrating no impact to murine body weight, no impacts to hematology cell counts or visible organ toxicities – necropsy and clinical pathology findings did not reveal any abnormal observations. A maximum tolerated dose has not yet been identified with murine xenograft studies, having been performed up to 450 mg/kg orally for 14 days (CG preliminary toxicity data).

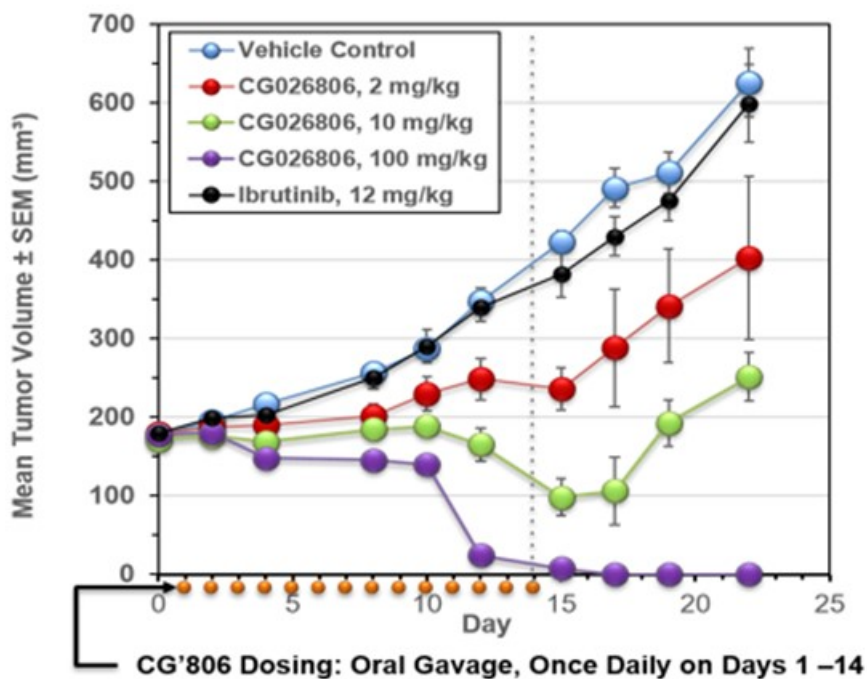


Figure 1a. Efficacy of CG-806 in MV4-11 xenograft model.

MV4-11 tumor bearing mice were administered an oral suspension once daily for 14 days of CG-806 at 2 mg/kg (blue line), 10 mg/kg (green line) or 100 mg/kg (red line), Ibrutinib, 12 mg/kg (turquoise line), or vehicle (Control; black line) with 7-day post-treatment follow-up. Tumor volumes and body weights were measured 3 times weekly.

In a separate MV4-11 xenograft study (Figure 1b), the antitumor efficacy of CG-806 was evaluated when mice were treated orally for 28 consecutive days with CG 806 at dose levels of 0 (black spheres), 10 (royal blue spheres), 30 (green spheres), 100 (grey spheres), or 300 mg/kg (light blue spheres). In this study, the clinical presentation (CG-806 co-micronized with 2.5% sodium laurth sulfate (SLS) ) and the dosing schedule ("BID") planned for human clinical studies were utilized. CG-806 effectively suppressed leukemia growth in MV4-11 AML at all doses through the 28-day period of dosing (Study Days 14-42 of the study). Administration of each dose level resulted in tumor growth inhibition ("%TGI") of at least 96% on Study Day 34 (last day that all vehicle control animas remained on study). Following termination of dosing with the 100 and 300 mg/kg dose levels, the tumors had not grown back after Study Day 60 of the study. Moreover, no signs of toxicity were noted at any dose level.

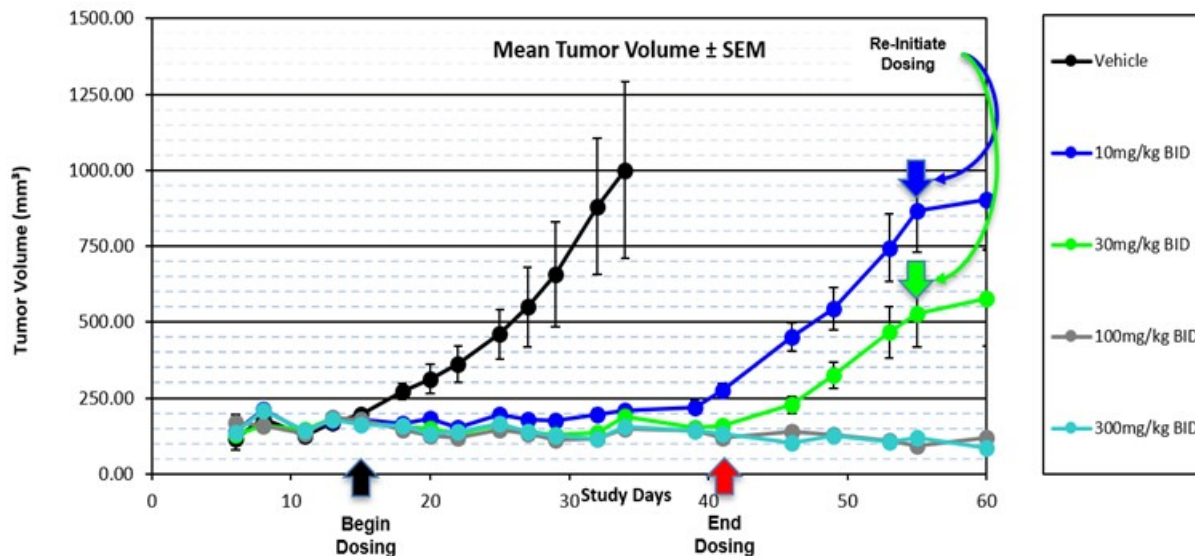


Figure 1b. Inhibition of Tumor Growth in MV4-11 AML Xenograft Mouse Model Following Oral BID Dosing for 28 Consecutive Days

Although the above murine xenograft models demonstrate potent antitumor activity with no observed toxicity, the models utilize an AML cell line rather than cells derived from an AML patient. In a study performed at the University of Texas MD Anderson Cancer Center ("MDACC"), the efficacy of CG-806 was evaluated in a patient derived xenograft ("PDX") model (Figure 1c). Bone marrow cells were collected from an AML patient that had relapsed on a clinical trial. The patients entered the trial with FLT3-ITD AML and was placed on sorafenib and azacytidine. After one cycle the patient had a complete response but then relapsed after cycle 3. Genetic analysis demonstrated that the AML cells had acquired a second mutation in AML, and this was the D835Y mutation, making the patient dual mutant FLT3-ITD/D835Y. Bone marrow cells from the patient (AML FLT3-ITD/D835) were implanted in mice to establish a PDX model. Expansion of the human AML cells in the bone marrow and peripheral blood of the mice took approximately one month. In the vehicle (15% Transcutol HP/85% PEG-400) treated mice, the leukemic burden in the peripheral blood increased from day 31 through day 50 and beyond. However, treatment with 100 mg/kg CG-806 (orally daily for 5 consecutive days followed by 2 days off every week), resulted in significant reduction in the leukemic burden and reductions in splenomegaly at 52 days post-implantation. These data suggest CG-806 may be used to treat patients that have become resistant to other FLT3 inhibitors.



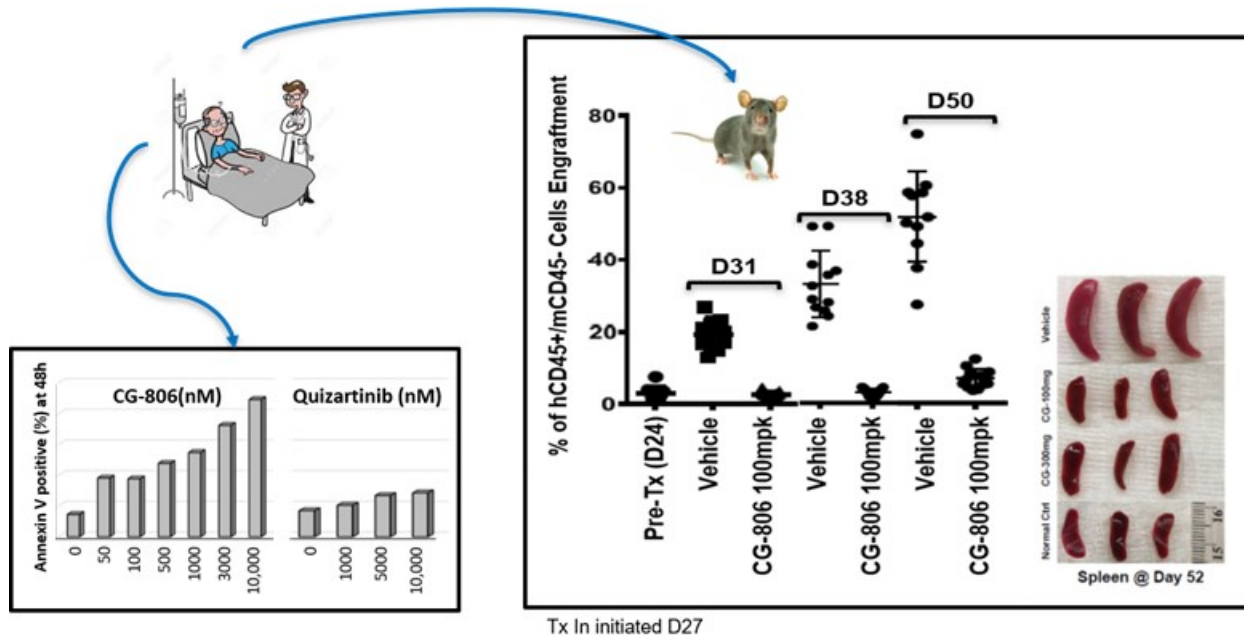


Figure 1c. CG-806 Efficacy in PDX Model Against AML Patient Cells with FLT3-ITD+D835Y Mutations

#### CG-806 Intellectual Property

A Patent Cooperation Treaty (“PCT”) application providing composition of matter and use protection for CG-806 was filed in late 2013, with a potential expiry in 2033 before extension opportunities, across all major geographies.

European Patent No. EP2940014B1

The granted patent claims the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and uses for treating diseases caused by abnormal or uncontrolled activation of protein kinases, such as cancer. This European patent will be nationalized in, and cover, approximately forty European countries including the United Kingdom, France, Germany, Italy, Netherlands and Spain. The patent is expected to provide protection until the end of 2033.

Australian Patent No. 2013371146

The granted patent claims numerous compounds, including the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and methods of treating various diseases. The patent is expected to provide protection until December of 2033.

Chinese Patent No. CN 104995184 B

The granted patent claims numerous compounds, including the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and the use of such a compound for the manufacture of a pharmaceutical composition for treating a disease caused by an abnormal or uncontrolled protein kinase. The patent is expected to provide protection until December of 2033.

Japanese Patent No. 6325573

The granted patent claims numerous compounds, including the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and the use of such a compound for the manufacture of a pharmaceutical composition for treating a disease caused by an abnormal or uncontrolled protein kinase. The patent is expected to provide protection until December of 2033.

#### CG-806 Manufacturing and Preclinical Progress

We have invested significant time, effort and capital to create a scalable chemical synthetic route for the manufacture of CG-806 drug substance, to develop an oral formulation for clinical development, and to study the actions of CG-806 in various preclinical biological pathway studies. Our efforts to develop the scalable chemical synthetic route have taken longer than anticipated and thus pushed the timeline for the IND submission and initiation of the first-in-human Phase I clinical trial further into the future than we had originally anticipated. We have solved the synthetic route, can scale the manufacture of the active pharmaceutical ingredient (API), and have manufactured and delivered a batch of API which was used for Dose Range Finding Studies that were performed and completed during 2018. In March 2018, we completed the manufacture of a multi-kg batch of GLP grade API and then formulated that API into a drug product for use in IND-enabling GLP toxicology studies. In addition, we completed a multi-kg batch of Good Manufacturing Practice (GMP) grade API for use in our planned first-in-human clinical trials and we manufactured, under GMP conditions, two dosage strengths of capsules intended to serve as our clinical supply in planned human studies. CG-806 is being developed with the intent to deliver the agent as an oral therapeutic and to develop it in parallel for AML and for appropriate B-cell malignancies (likely CLL). As clinical trials are lengthy, complex, costly, and uncertain processes, an estimate of the future costs is not reasonable at this time.

During 2018, Aptose performed a comprehensive package of studies to characterize the absorption, distribution, and metabolism properties of CG-806, and the potential for pharmacokinetic drug interactions. Single-dose oral and intravenous (“IV”) pharmacokinetic (“PK”) studies were conducted in mice, rats, and dogs; these studies were primarily performed to support selection of the most appropriate rodent species and a suitable formulation for the GLP toxicology studies. Repeat-dose oral toxicokinetic (“TK”) studies were conducted in mice and dogs. An in vitro plasma protein binding study, an in vitro metabolic profiling study, and a cytochrome P450 (“CYP”) phenotyping study were also conducted. Additionally, metabolism-based drug-interaction studies evaluated the ability of CG-806 to be an inhibitor of CYP enzymes, as well as the potential to be a substrate or inhibitor of transporter proteins. The results of these nonclinical studies continue to support the development of CG-806 and do not indicate safety concerns for the development of CG-806.

Aptose conducted GLP toxicology studies (28-day BID oral dosing in rodents and dogs), and a series of secondary GLP safety studies. These studies revealed CG-806 to be a well-tolerated molecule. Mice were chosen as the rodent species because they achieved higher plasma exposure levels than rats, and this allowed for a more accurate assessment of potential toxicities. CG-806 was administered by oral gavage twice daily at levels up to 300 mg/kg BID (600 mg/kg/day) to mice and up to 120 mg/kg BID (240 mg/kg/day) to dogs. The BID dose schedule was selected to increase exposures and elicit toxicity. Cardiovascular endpoints were incorporated into the GLP 28-day dog toxicity study, and CG-806 showed no effects on cardiovascular function (ECG measures and cardiac parameters) in dogs at any dose. In these GLP studies, no adverse events related to CG-806 were noted in mice or dogs at the highest doses that could be feasibly administered.

Because other kinase inhibitors have been reported to cause cardiovascular events, a separate GLP dog cardiovascular safety study was performed with CG-806, and an alternate formulation was used to boost plasma exposures and reveal any potential cardiovascular safety concerns. In this study, using a telemetry system with male Beagle dogs, no effects on cardiovascular parameters were noted at any dose level of CG-806. A series of secondary GLP safety studies were performed to further understand the molecule. Single oral doses of CG-806 had no acute effects on the central nervous system (“CNS”) or the respiratory system in male CD-1 mice administered a single oral dose. Also, CG-806 was not mutagenic in a GLP bacterial reverse mutation (Ames) assay.

On April 15, 2018 at the 2018 Annual Meeting of the American Association for Cancer Research (“AACR”), we presented with the OHSU Knight Cancer Institute preclinical data demonstrating that CG-806, a pan-FLT3/pan-BTK inhibitor, demonstrates broader activity and superior potency to other FLT3 and BTK inhibitors against primary bone marrow samples from patients with hematologic malignancies. We also presented preclinical data demonstrating CG-806 targets multiple pathways to kill diverse subtypes of AML and B-cell malignancies in vitro.

On June 15, 2018 at the 23rd Congress of the European Hematology Association (“EHA”), we presented, during a poster presentation, preclinical data demonstrating CG-806 unique binding to wild type and C481S mutant BTK. Further, we presented that CG-806 inhibits the BCR, AKT/PI3K, ERK and NFkB signaling pathways and exerts broader and far greater potency than Ibrutinib against malignant bone marrow cells from patients with CLL, ALL and a host of other hematologic malignancies.

On December 3, 2018 at the 60th American Society of Hematology (“ASH”) Annual Meeting, we presented in a poster presentation with the OHSU Knight Cancer Institute preclinical, data demonstrating that CG-806 exhibits broad ex vivo potency on bone marrow cells from patients with CLL and other B-cell cancers. In a separate poster presentation, we presented with the University of Texas MD Anderson Cancer preclinical data demonstrating that CG-806 overcomes the emergence of resistance common to other FLT3 inhibitors.

On February 22, 2019 we announced that we had submitted an IND application for CG-806 to the FDA requesting approval to initiate a Phase 1 clinical trial program. Pending regulatory allowance, Aptose plans to conduct a Phase 1 trial with orally administered CG-806 in patients with relapsed or refractory B cell malignancies, including CLL/SLL and NHL who failed or are intolerant to standard therapies. Pending the collection of predictive pharmacokinetic data in humans, Aptose would seek allowance from the FDA to move into the AML/MDS patient population in a separate Phase I trial. The initial goal of both trials is to evaluate safety, tolerability and pharmacokinetics of CG-806 in these patient populations.

## **APTO-253 Program**

### *Overview*

APTO-253, the Company's second program, 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. The MYC oncogene is overexpressed in hematologic cancers, including AML. MYC is a transcription factor that regulates cell growth, proliferation, differentiation and apoptosis, and overexpression amplifies new sets of genes to promote oncogenesis. APTO-253 dramatically down-regulates expression of the MYC oncogene in AML cells and depletes those cells of the MYC oncoprotein, leading to apoptotic cell death in AML cells. Thus APTO-253 may serve as safe and effective MYC inhibitor for AML that combines well with other agents and does not impact the normal bone marrow.

We were evaluating APTO-253 in a Phase Ib clinical trial in patients with relapsed / refractory hematologic malignancies, particularly AML and MDS, before being placed on clinical hold by the FDA in November 2015. The Phase Ib trial was placed on clinical hold in order to solve a chemistry-based formulation issue, and the chemistry of the API and the formulation had undergone minor modifications to deliver a stable and soluble drug product for return to the clinical setting. In December 2016, we announced that we had successfully manufactured multiple non-GMP batches of a new drug product formulation for APTO-253, including a batch that had been stable and soluble for over six months. However, the 40L batch that was the intended clinical supply encountered an unanticipated mishap during the filling process that compromised the stability of that batch of drug product. On January 23, 2017, we announced that the root cause and corrective action studies would take longer than originally expected and that we would temporarily delay clinical activities with APTO-253 in order to elucidate the cause of manufacturing setback, with the intention of restoring the molecule to a state supporting clinical development and partnering. Formal root cause analyses studies were completed and identified the reason for the drug product stability failure. We manufactured a new GMP clinical supply of drug product and performed the studies required to demonstrate the fitness of the drug product for clinical usage, and presented the findings to the FDA in the second quarter of 2018. On June 28, 2018, the FDA notified us that it had lifted the clinical hold on APTO-253. This was followed by resubmission of the revised clinical protocol to Institutional Review Boards ("IRB") at multiple clinical sites.

On November 28, 2018 we announced that we dosed the first patient in the re-initiation of the Phase Ib Clinical Study of APTO-253. In January 2019, we provided data on the Aptose website that we observed meaningful reductions in MYC expression in the PBMC from the first patient dosed with the new formulation of APTO-253.

### *APTO-253 Studies on Solid Tumors*

In January 2011, Aptose announced the first patient enrollment in a Phase I dose-escalation study for APTO-253 in patients with advanced or metastatic solid tumors who are unresponsive to conventional therapy or for whom no effective therapy is available. The study was initially being conducted at Memorial Sloan-Kettering Cancer Center in New York. Objectives of the study included determination or characterization of the safety profile, maximum tolerated dose, and antitumor activity of APTO-253, as well as pharmacokinetics and a recommended Phase II dose for subsequent clinical trials.

In June 2012, MD Anderson Cancer Center in Houston was added as a second site under the direction of Dr. Jennifer Wheeler as the principal investigator. In addition, Aptose announced that the study had successfully completed the accelerated drug dose escalation stage (Stage 1), with further escalation under way in the non-accelerated dose escalation stage (Stage 2) for the purpose of determining the maximal tolerated dose level and recommended Phase II dose. The addition of a second site expanded patient availability for enrollment.

In January 2013, Aptose announced that Phase I clinical study of APTO-253 had successfully escalated to the target dose level based on predicted and observed clinical effects without limitation by toxicity. The success of this study allowed Aptose to initiate a biomarker clinical investigation to further explore the effects of the drug at relevant doses determined in the clinical trial.

In April 2013, Aptose announced that studies demonstrated the antitumor activity of APTO-253 in animal models of human NSCLC with a dose-response effect in NSCLC.

In July 2013, Aptose announced the results of the Phase 1 clinical trial of APTO-253. In this first-in-man dose-escalation clinical study, APTO-253 demonstrated a favorable safety profile, as well as encouraging signs of antitumor activity. The design of this trial consisted of APTO-253 as a single agent in patients with advanced solid tumors resistant to multiple standard therapies. The study enrolled 27 patients, all of which had failed a median of four prior chemotherapies. Although this was primarily a dose-escalation safety study, efficacy and pharmacokinetics were also explored.

The clinical trial enrolled patients at seven dose levels ranging from 20 to 229 mg/m<sup>2</sup>. Of the 27 patients enrolled, 17 were evaluable for efficacy. Of these 17 patients, seven (41%) achieved stable disease by Response Evaluation Criteria In Solid Tumors (“RECIST”). This included patients with colorectal, lung, appendiceal, liver and uterine cancers. Dose related activity was demonstrated at the higher dose levels (176 and 229 mg/m<sup>2</sup>). At these two highest dose levels, four of five evaluable patients (80%) achieved sustained stable disease by RECIST ranging from 5.6 months to 8 months, representative of disease control. Of these, a patient with non-small cell lung cancer at the highest dose level additionally demonstrated non-index tumor shrinkage.

The safety assessment indicated that APTO-253 was well tolerated at all dose levels tested in this trial. The dose escalation was not limited by toxicity. The most common adverse event was Grade 1 or 2 fatigue seen in three patients. There was one Grade 3 toxicity, asymptomatic low blood phosphate level that was reversible by supplementation with phosphates. The pharmacokinetic profile was consistent with the predictive profile seen preclinically, and the elimination profile and half-life in patients were suggestive of a very rapid distribution phase and prolonged retention.

#### **Multi-Targeting Bromodomain Program**

In November 2015, Aptose entered into a definitive agreement with Moffitt Cancer Center (“Moffitt”) for exclusive global rights to potent, multi-targeting, single-agent inhibitors for the treatment of hematologic and solid tumor cancers. These small molecule agents are inhibitors of the Bromodomain and Extra-Terminal motif (“BET”) protein family members, which simultaneously target specific kinase enzymes. The molecules developed by Moffitt exhibited potency against the BET family members and specific oncogenic kinases which, when inhibited, are synergistic with BET inhibition. Under the agreement, Aptose would gain access to the drug candidates developed by Moffitt and the underlying intellectual property covering the chemical modifications enabling potent bromodomain (“BRD”) inhibition on the chemical backbone of a kinase inhibitor.

In January 2017, Aptose terminated the collaboration with Moffitt for the development of the dual BRD4 / JAK2 inhibitor program.

#### **Multi-Targeting Epigenetic Program**

In November 2015, Aptose announced an exclusive drug discovery partnership with Laxai Avanti Life Sciences (“LALS”) for their expertise in next generation epigenetic-based therapies. Under the agreement, LALS was to be responsible for developing multiple clinical candidates, including optimizing candidates that exert dual BRD4 / kinase inhibitory activity. Based on available resources, Aptose halted further investment in the collaboration with LALS in late 2016. However, the program delivered novel intellectual property and hit molecules for further optimization. As a consequence, Aptose may choose to out-license the program.

On March 7, 2018, we entered into an exclusive global license agreement with Ohm Oncology (“OHM”), an affiliate of LALS that was formed in 2016 to advance the clinical development of compelling molecules derived from the LALS initiative, for the development, manufacture and commercialization of APL-581, as well as related molecules, from Aptose’s dual BET protein and kinase inhibitor program. Under the agreement, Aptose retained reacquisition rights to certain molecules, while OHM/LALS has the rights to develop and sublicense all other molecules. Aptose received a nominal upfront cash payment and is eligible to receive up to \$125 million of additional payments based on the achievement of certain developmental, regulatory and sales milestones, as well as significant royalties on future sales generated from the program, if any.

#### **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 into 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.

CG-806

### *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 the C481S-mutant forms. Companies that have developed approved or are currently developing inhibitors that directly target the wild type include AbbVie (IMBRUVICA) and AstraZeneca (CALQUENCE) and Beigene Co., Ltd., (Zanubrutinib).

Others that are developing inhibitors that target the C481S-mutant BTK include Arqule, Inc. (ARQ 531), Roche, Sunesis Pharmaceuticals (SNS-062) and Eli Lilly amongst others.

Other companies that are currently developing BTK BCL2 inhibitors include Gilead, GlaxoSmithkline, Merck KGaA., Principia Biopharma and AbbVie amongst others.

CG-806 and APTO-253

### *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 or are currently developing non-targeted therapies include Jazz (VYXEOS), Pfizer (MYLOTARG) and Roche (VENCLEXTA), among others. Others that have developed or are developing highly targeted therapies such as FLT-3 include Novartis (RYDAPT), Astellas (XOSAPTA), Daiichi Sankyo (QUIZARTINI), Arog (CRENOLANIB), and IDH1 include Agios (TIBSOVO) and IDH2 include Celgene/BMS (IDHIFA) 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 of 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.

CG-806

On September 12, 2017, we announced that United States Patent and Trademark Office (“USPTO”) issued patent number 9,758,508 entitled “2,3-dihydro-isoindole-1-on derivative as BTK kinase suppressant, and pharmaceutical composition including same”. The patent claims numerous compounds, including the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and methods of treating various diseases. The patent is expected to provide protection until December of 2033.

On July 10, 2018, we announced that Japanese Patent Office issued patent number 6325573 for CG-806. The patent claims numerous compounds, including the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and the use of such a compound for the manufacture of a pharmaceutical composition for treating a disease caused by an abnormal or uncontrolled protein kinase. The patent is expected to provide protection until December of 2033.

In 2018, we acquired the exclusive licensing rights to Chinese Patent No. CN 104995184 B. This patent claims numerous compounds, including the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and the use of such a compound for the manufacture of a pharmaceutical composition for treating a disease caused by an abnormal or uncontrolled protein kinase. The patent is expected to provide protection until December of 2033.

On September 27, 2018, we announced that the European Patent Office issued European Patent Number EP2940014B1 for CG-806. The patent claims various compounds, including the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and uses for various diseases, such as cancer. The patent has been validated in 22 European countries, and is expected to provide protection until December of 2033.

On March 4, 2019, we announced that the Australian Patent Office issued Australian Patent Number 2013371146 for CG-806 entitled “2,3-dihydro-isindole-1-on derivative as BTK kinase suppressant, and pharmaceutical composition including same”. The patent claims numerous compounds, including the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and methods of treating various diseases. The patent is expected to provide protection until December of 2033.

#### APTO-253

As of March 12, 2019, we are the owner of record of five issued U.S. patents, which together provide coverage for the APTO-253 compound, its pharmaceutical composition and methods of treating various cancers with APTO-253, including solid tumors and leukemia. The APTO-253 composition of matter has patent protection until February, 2028 in the United States and May, 2026 in other countries. We also hold 20 international (non-U.S.) patents which together provide coverage for APTO-253, three of which are issued European patents, validated in at least eight countries in Europe. Our patents also include several compounds that are similar to APTO-253, which provide protection from competitors seeking to develop anticancer products that are related in chemical structure to APTO-253.

#### 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 at December 31, 2018, we employed 22 full-time persons and two part-time persons in research and drug development and administration activities. Four of our employees hold Ph.D.’s and numerous others hold degrees and designations such as MSc, BSc, CPA (CA), CPA-Inactive (California) and MBA. 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 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 current GMP(s) 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. These committees are called 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 I 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 II and III involve therapeutic studies. In Phase II, 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 III, 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 III, 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 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 labelling, 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 a 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 IND submission, similar to that required for a clinical trial application in Canada. Clinical trials with human subjects are characterized as Phase I, Phase II and Phase III 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. These committees are called 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 IV 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 IV 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 brief summary of the requirements for a new drug to be approved for marketing in North America. The European Medicines Agency 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.

### **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 Chairman and Chief Executive Officer and our Chief Financial Officer.

Dr. William G. Rice, age 60, joined Aptose as Chairman and Chief Executive Officer in October 2013. Prior to joining Aptose, Dr. Rice served as the President, Chief Executive Officer and Chairman of the board of Cylene Pharmaceuticals, Inc., a private biotechnology company ("Cylene") 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. He continues to serve as the Chairman of the board of Cylene and is a member of the board of directors of Oncolytics Biotech Inc.

Gregory K. Chow, age 46, joined Aptose as Chief Financial Officer in December 2013. Previously, Mr. Chow served as Managing Director, Director of Private Placements at Wedbush Securities from 2012 to 2013, where he led the private placement capital activities within the Life Sciences Investment Banking Group. Prior to joining Wedbush, he was a Director in the Private Placements / Equity Capital Markets Group at RBC Capital Markets from 2006 to 2011, where he led life science private capital activities. From 2003 to 2006, he led the Private Capital Group at Wells Fargo Securities and was a Senior Auditor at BDO Seidman, LLP in their Century City, CA office. Mr. Chow is a Certified Public Accountant (inactive) in the State of California. Mr. Chow received his MBA in Finance from The Wharton School at the University of Pennsylvania, and his BA in Business Economics with an emphasis in Accounting from the University of California, Santa Barbara.

### **Corporate Information**

Aptose is a publicly traded company incorporated pursuant to the Canada Business Corporations Act, or CBCA. Our headquarters are located at 251 Consumers Road, Suite 1105 Toronto, Ontario, Canada M2J 4R3 (telephone: 647-479-9828).

We file annual, quarterly, current reports, proxy statements and other information with the Securities and Exchange Commission (the "SEC"). We make available free of charge at our website <http://www.aptose.com> (under the "Investors — Financial Information" caption) all of our reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, including our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K and amendments to those reports. Prior to December 31, 2018, Aptose was a foreign private issuer, and in compliance with SEC regulations, filed its Quarterly reports on Form 6-Ks, and its Annual Reports on either Forms F-20 or F-40. These reports are made available on our website as soon as reasonably practicable after their filing with, or furnishing to, the SEC. The SEC maintains an internet site that contains our public filings with the SEC and other information regarding the Company, at [www.sec.gov](http://www.sec.gov). We are also a reporting issuer under the securities laws of the Province of Ontario in Canada.

### **Cautionary Note Regarding Forward-Looking Statements**

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;
- 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. 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 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 United States Food and Drug Administration, or “FDA”, or other similar foreign regulatory agency that we are required to report to, may ultimately not approve any of our product candidates;
- 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, 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;
- 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 “emerging growth company” and “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 the common shares to Aspire Capital pursuant to the purchase agreement between us and Aspire;
- any failure of Aspire to purchase common shares from us when required to do so;
- 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.

More detailed information about these and other factors is included in this Annual Report on Form 10-K under Item 1A. Risk Factors. 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.

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. **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**

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

We are at an early stage of development. In the past five years, none of our potential products has obtained regulatory approval for commercial use and sale in any country and as such, no significant 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 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. We also do not know whether sales, license fees or related royalties will allow us to recoup any investment we make in the commercialization of our products.

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. For example, our product candidate APTO-253 began enrollment in a Phase Ib clinical trial in patients with relapsed or refractory AML and high risk MDS and was placed on clinical hold by the FDA following a voluntary suspension of dosing by us. That hold has been lifted, but significant additional funding will be necessary to complete the restarted Phase Ib clinical and, if required, Phase II or Phase III 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 would likely 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.

***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 \$28.8 million in the fiscal year ended December 31, 2018, \$11.7 million in the fiscal year ended December 31, 2017, and \$14.2 million in the fiscal year ended December 31, 2016, and as of December 31, 2018, we had an accumulated deficit of \$276.0 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 APTO-253 or CG-806 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 Chief Executive Officer and our Chief Financial Officer, 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 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 in the future 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.

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 short-term or long-term benefits 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 would 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 United States dollar against certain other currencies because we hold most of our cash and cash equivalents in United States 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**

***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.***

In the past five years, 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 effectiveness of our product candidates before we can submit any regulatory applications.

Clinical trials are long, expensive and uncertain processes. Clinical trials may not be commenced or completed on schedule and the FDA or Health Canada or any other regulatory body may not ultimately approve our product candidates for commercial sale. 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 I clinical trials may not be repeated in larger Phase II or Phase III 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. For example, our Phase Ib clinical trial of APTO-253 in patients with relapsed or refractory AML and high risk MDS was placed on clinical hold by the FDA in November 2015 and since that time the Company has encountered manufacturing setbacks which further delayed the return of APTO-253 to the clinic. There can be no assurance that the Company will have the resources, or that we will decide, to continue the development of APTO-253. Even if the Phase Ib of APTO-253 is continued, there is a long development path ahead that will take many years to complete and is prone to the risks of failure or delays inherent in drug development. Likewise, our CG-806 product candidate has not yet entered clinical trials and it is expected to undergo many years of testing and regulatory examinations prior to any potential regulatory approvals.

Preparing, submitting and advancing applications for regulatory approval 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, 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 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 submission of an Investigational New Drug (“IND”) application, the commencement and completion of clinical trials 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. We may not make regulatory submissions or receive regulatory approvals as planned; our clinical trials may not be completed; 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, or 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 recommencement and completion of clinical trials for our products, including the APTO-253 phase I clinical trial and the IND acceptance and phase I clinical trial for CG-806, may be delayed for a number of reasons, including delays related, but not limited, to:

- failure by regulatory authorities to grant permission to proceed 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 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 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 for re-examination, which may impact the cost, timing or successful completion of that 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 contract manufacturing organizations (“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 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.

We contracted with multiple CMOs for the manufacture of APTO-253 and CG-806 to supply drug supply and then drug product for our clinical trials. The synthesis of CG-806 drug supply is challenging from a scale-up synthetic chemistry perspective. The formulation and manufacture of APTO-253 is a complex process with many variables involved. We pre-qualified CMOs to have the capacity, the systems and the experience to supply CG-806 and APTO-253 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 CG-806 and APTO-253. 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.

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

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 on a timely basis or at all. Certain factors that affect enrollment of patients onto 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.

***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, cancelled 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 II, Phase III 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 have substantial 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 III clinical trials or registration trials. The FDA, Health Canada or other regulatory authorities may disagree with our trial design and the Company's 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 III clinical trial that has the potential to result in FDA, Health Canada or other agencies' approval. In addition, any of these regulatory authorities may also approve a product candidate for fewer or more limited indications than the Company requests 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, and operate 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
- 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, such as 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 CG-806 and APTO-253 in AML, examples of potential competitors include Companies that have developed approved or are currently developing inhibitors that directly target the wild type include AbbVie (IMBRUVICA) and AstraZeneca (CALQUENCE) and Beigene Co., Ltd., (Zanubrutinib).

Others that are developing inhibitors that target the C481S-mutant BTK include Arqule, Inc. (ARQ 531), Roche, Sunesis Pharmaceuticals (SNS-062) and Eli Lilly amongst others.

For CG-806 and APTO-253 in AML, examples of potential competitors include companies that have developed approved or are currently developing non-targeted therapies include Jazz (VYXEOS), Pfizer (MYLOTARG) and Roche (VENCLEXTA), among others. Others that have developed or are developing highly targeted therapies such as FLT-3 include Novartis (RYDAPT), Astellas (XOSAPTA), Daiichi Sankyo (QUIZARTINIB), Arog (CRENOLANIB), and IDH1 include Agios (TIBSOVO) and Celgene/BMS (IDHIFA) 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 its 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 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 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 United States Patent and Trademark Office, 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 APTO-253 or CG-806. 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 CG, and are subject to significant obligations under that license agreement.***

The rights we hold under our license agreement with CG is critical to our business. Our CG-806 program is built around patents exclusively in-licensed from CG, which permit us to research, develop and commercialize CG-806 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 in all territories outside of the Republic of Korea.

If there is any conflict, dispute, disagreement or issue of non-performance between us and CG regarding our rights or obligations under the license agreements including any conflict, dispute or disagreement arising from our failure to satisfy diligence or payment obligations under such agreements, CG may have a right to terminate the 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 CG-806 worldwide except for the Republic of Korea. The license from CG is 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, product and market our products is subject to extensive government regulation.***

Government regulation is a significant factor in the development, production and marketing of the Company's 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 the Company's product candidates 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 warning letters, the imposition of civil penalties or other monetary payments, delay in approving or refusal to approve a product candidate, suspension or withdrawal of regulatory approval, product recall or seizure, operating restrictions, interruptions of clinical trials or manufacturing, injunctions or criminal prosecution. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of the Company's 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.

*Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and 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.

Members of Congress and the Trump Administration have considered legislation to fundamentally change or repeal the Affordable Care Act. While Congress has not passed repeal legislation to date, the Tax Cuts and Jobs Act (“TCJA”) includes a provision repealing the individual insurance coverage mandate included in the Affordable Care Act, effective January 1, 2019. Further, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, the President signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the Affordable Care Act. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, the Centers for Medicare and Medicaid Services has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the Affordable Care Act for plans sold through such marketplaces. Congress may consider other legislation to replace elements of the Affordable Care Act. The implications of the Affordable Care Act, its possible repeal, any legislation that may be proposed to replace the Affordable Care Act, or the political uncertainty surrounding any repeal or replacement legislation for our business and financial condition, if any, are not yet clear.

We cannot predict what healthcare reform initiatives may be adopted in the future. Further federal and state legislative and regulatory developments are likely, and we expect ongoing initiatives in the United States to increase pressure on drug pricing. Such reforms 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. 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.

***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 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 will expose us to broadly applicable U.S. and Canadian fraud and abuse and other healthcare laws and regulations 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 the Company's 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 the Company's development activities progress towards the commercialization of product candidates, our liability coverage may not be adequate, and the Company may not be able to obtain adequate product liability insurance coverage at a reasonable cost, if at all. Even if the Company obtains product liability insurance, its financial position may be materially adversely affected by a product liability claim. A product liability claim could also significantly harm the Company's reputation and delay market acceptance of its 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. Commencing Phase I, Phase II and Phase III clinical trials for CG-806 and continuing Phase Ib, and commencing Phase II and Phase III clinical trials for APTO-253 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:

- our ability to continue as a going concern;
- our ability to raise additional capital;
- 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;
- public concern as to the safety and efficacy of drugs that we and our competitors develop;
- shareholder interest in our Common Shares; and
- low liquidity in the daily trading volume of our Common Shares.

***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.

***An active trading market in our Common Shares may not be sustained.***

Our Common Shares are listed for trading on the Nasdaq Capital Market and the TSX. However, an active trading market in our Common Shares on the stock exchanges may not be sustained and we may not be able to maintain our listings.

***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.

#### **Other 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 officers, and many of the experts named 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 the Company believes it was classified as a passive foreign investment company ("PFIC") during the tax year ended December 31, 2017, 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, the Company expects to be a PFIC for the current tax year ending December 31, 2018 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.

***We are an “emerging growth company,” and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our Common Shares less attractive to investors.***

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012 (United States), or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 (United States) (the “SOX”), reduced disclosure obligations regarding executive compensation in our periodic reports and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We will cease to be an emerging growth company upon the earliest of:

- the last day of the fiscal year during which we have total annual gross revenues of \$1,000,000,000 (as such amount is indexed for inflation every five years by the United States Securities Exchange Commission (the “SEC”) or more;
- the last day of our fiscal year following the fifth anniversary of the completion of our first sale of common equity securities pursuant to an effective registration statement under the Securities Act (United States) which will be in September 2020;
- the date on which we have, during the previous three-year period, issued more than \$1,000,000,000 in non-convertible debt; or
- the date on which we are deemed to be a “large accelerated filer”, as defined in Rule 12b-2 of the Exchange Act (United States) (the “Exchange Act”), which would occur if the market value of our ordinary shares that are held by non-affiliates exceeds \$700,000,000 as of the last day of our most recently-completed second fiscal quarter.

We cannot predict if investors will find our Common Shares less attractive because we may rely on these exemptions. If some investors find our Common Shares less attractive as a result, there may be a less active trading market for our Common Shares and our share price may be more volatile.

***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 SOX requires that our management assess and report annually on the effectiveness of our internal controls over financial reporting and identify any material weaknesses in our internal controls over financial reporting. Although Section 404(b) of the SOX requires our independent registered public accounting firm to issue an annual report that addresses the effectiveness of our internal controls over financial reporting, we have opted to rely on the exemptions provided to us by virtue of being an emerging growth company, and consequently will not be required to comply with SEC rules that implement Section 404(b) of SOX until we lose our emerging growth company status.

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 International Financial Reporting Standards, as issued by the International Accounting Standards Board, 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.

***Prior to December 31, 2018, we were a foreign private issuer and were therefore not subject to certain United States securities law disclosure requirements that apply to a domestic United States issuer, which may limit the historical information publicly available to our shareholders.***

As a foreign private issuer prior to December 31, 2018, we were exempt from certain rules under the Exchange Act that impose disclosure requirements as well as procedural requirements for proxy solicitations under Section 14 of the Exchange Act. In addition, our officers, directors and principal shareholders were exempt from the reporting and “short-swing” profit recovery provisions of Section 16 of the Exchange Act. Moreover, we were not required to file periodic reports and financial statements with the SEC as frequently or as promptly as a company that files as a domestic issuer whose securities are registered under the Exchange Act, nor were we generally required to comply with the SEC’s Regulation Fair Disclosure, which restricts the selective disclosure of material non-public information. For as long as we were a “foreign private issuer” we filed our annual financial statements on Form 20-F and furnished our quarterly updates on Form 6-K to the SEC. However, the information we filed or furnished was not the same as the information required in annual and quarterly reports on Form 10-K or Form 10-Q for United States domestic issuers. Accordingly, there may be less historical information publicly available concerning us than there is for a company that has filed as a domestic issuer for longer.

***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 Aptose’s business. In particular, a cyber security incident could result in the loss or corruption of data from Aptose’s research and development activities, including clinical trials, which may cause significant delays to some or all of the Company’s clinical programs. Also, the Company’s trade secrets, including unpatented know how, technology and other proprietary information could be disclosed to competitors further to a breach, which would harm the Company’s 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 the Company 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 approximately 7,309 of office space and 1,876 lab space in San Diego, California. The lease for the office space expires on March 31, 2023 and can be extended for an additional 5 year period. The lease for our lab space expired on February 29, 2019, and on February 18, 2019 was renewed until February 28, 2022. We lease approximately 2,078 of office space in Toronto, Ontario, Canada. The lease for this location expires on June 30, 2023 with an option to renew for another 5-year period. 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 are not currently party to any material legal proceedings.

## **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".

### Holder of Record

As of March 12, 2019, there were approximately 29 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. as one shareholder.

### Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

### Repurchases of Equity Securities

There were no repurchases of equity securities during the fourth quarter of 2018.

## **ITEM 6. SELECTED FINANCIAL DATA**

The following selected consolidated financial data have been derived from, and should be read in conjunction with, the accompanying audited consolidated financial statements for the years ended December 31, 2018 and 2017, respectively, and related notes appearing elsewhere in this Annual Report on Form 10-K (the "Financial Statements") which are prepared in accordance with US GAAP. You should read the selected financial data set forth below in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes included elsewhere in this Annual Report on Form 10-K.

**Consolidated Statements of Loss and Comprehensive Loss**

<i>(amounts in US thousands except for per common share data)</i>	Year ended December 31, 2018	Year ended December 31, 2017
<b>REVENUE</b>	\$ —	\$ —
<b>EXPENSES</b>		
Research and development	18,733	6,274
General and administrative	10,374	5,552
<b>Operating expenses</b>	<b>29,107</b>	<b>11,826</b>
Interest Income	283	68
Foreign exchange gains/(losses)	(44)	115
<b>Total other income</b>	<b>239</b>	<b>183</b>
<b>Net loss</b>	<b>(28,868)</b>	<b>(11,643)</b>
<b>Other comprehensive loss:</b>		
Unrealized (gain)/losses on securities available-for-sale	—	18
<b>Total comprehensive loss</b>	<b>(28,868)</b>	<b>(11,661)</b>
<b>Basic and diluted loss per common share</b>	<b>\$ (0.86)</b>	<b>\$ (0.52)</b>
<b>Weighted average number of Common Shares outstanding used in the calculation of:</b>		
<b>Basic and diluted loss per share</b>	<b>33,391</b>	<b>22,313</b>
<b>Total Assets</b>	<b>\$ 16,870</b>	<b>\$ 11,967</b>
<b>Total Long-term Liabilities</b>	<b>\$ —</b>	<b>\$ —</b>

**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.

**OVERVIEW**

Aptose Biosciences is a science-driven biotechnology company advancing first-in-class agents to treat life-threatening cancers, such as acute myeloid leukemia (AML), high-risk myelodysplastic syndromes (MDS), chronic lymphocytic leukemia (CLL) and other hematologic malignancies. Based on insights into the genetic and epigenetic profiles of certain cancers and patient populations, Aptose is building a pipeline of novel oncology therapies directed at dysregulated processes and signaling pathways. Aptose is developing targeted medicines for precision treatment of these diseases, based on a patient's specific gene expression signature. In the treatment of cancer, this strategy is intended to optimize efficacy and quality of life by minimizing the cytotoxic side effects associated with conventional therapies. We currently have in development two molecules: CG-806 and APTO-253 which are described below.

CG026806 (CG-806) is an oral, highly potent first-in-class pan-FLT3/pan-BTK inhibitor. Development of CG-806 is intended for the treatment of patients having B-cell malignancies including chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL) and certain non-Hodgkin's lymphomas that are resistant/refractory/intolerant to other therapies, as well as for patients with relapsed/refractory Acute Myeloid Leukemia (R/R AML), including the emerging populations resistant to FLT3 inhibitors. CG-806 is a highly potent, reversible, non-covalent inhibitor of the wild type and mutant forms of the BTK enzymes. Overexpression of BTK drives certain B cell malignancies, and treatment of such B cell malignancies with covalent BTK inhibitors that target the cysteine residue in the active site of BTK can lead to drug resistance via mutation of the cysteine amino acid residue to a serine residue (BTK-C481S mutant). CG-806 targets the ATP-binding pocket of BTK through a reversible, non-covalent mechanism, thereby allowing CG-806 to retain low nM potency against the BTK-C481S mutant enzyme. Thus, CG-806 may serve as a novel therapeutic agent to treat B cell malignancy patients that are refractory, resistant or intolerant to covalent BTK inhibitors and other non-covalent BTK inhibitors currently in development. In addition to potent inhibition of wild type and mutant forms of the BTK enzyme, CG-806 exhibits a picomolar IC50 toward the FMS-like tyrosine kinase 3 with the Internal Tandem Duplication (FLT3-ITD) and significant potency against all other mutant forms of FLT3. Because of the potency of CG-806 against the FLT3 enzyme, it may become an effective therapy for AML patients, including the subset of patients having the FLT3-ITD, which occurs in approximately 30% of patients with AML and is associated with poor prognosis. Importantly, CG-806 targets other oncogenic kinases which may also be operative in AML, thereby potentially allowing the agent to become an important therapeutic option for a difficult-to-treat patient population.

APTO-253, the Company's IND-stage program, is a small molecule therapeutic agent that inhibits expression of the MYC oncogene without causing general myelosuppression of the bone marrow. The MYC oncogene is overexpressed in hematologic cancers, including AML and CLL. MYC is a transcription factor that regulates cell growth, proliferation, differentiation and apoptosis, and overexpression amplifies new sets of genes to promote oncogenesis. APTO-253 downregulates expression of the MYC oncogene in AML cells and depletes those cells of the MYC oncoprotein, leading to apoptotic cell death in AML cells. Thus APTO-253 may serve as a safe and effective MYC inhibitor for AML that combines well with other agents and does not impact the normal bone marrow.

## PROGRAM UPDATES

### *CG-806*

On February 22, 2019, we announced that we had submitted an Investigational New Drug (IND) application for CG-806 to the U.S. Food and Drug Administration (FDA) requesting approval to initiate its Phase 1 clinical trial program. Pending regulatory allowance, Aptose plans to conduct a Phase 1 trial with orally administered CG-806 in patients with relapsed or refractory B cell malignancies, including CLL/SLL and non-Hodgkin lymphomas (NHL) who failed or are intolerant to standard therapies. Pending the collection of predictive pharmacokinetic data in humans, Aptose would seek allowance from the FDA to move into the AML/MDS patient population in a separate Phase I trial. The initial goal of both trials is to evaluate safety, tolerability and pharmacokinetics of CG-806 in these patient populations.

In May 2018, we paid \$2.0 million in cash and obtained 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 South Korean company CrystalGenomics, Inc. ("CG"), granting us an exclusive option to research, develop and commercialize (collectively the "Rights") CG026806 ("CG-806"). We paid \$1.0 million to CG to acquire the option.

In June 2018, we entered into a separate license agreement with CG for Aptose to gain a license for Rights to CG-806 in 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 payments upon the achievement of developmental, regulatory and commercial-based milestones, as well as single-digit royalties on product sales in China. Aptose now owns worldwide Rights to CG-806, including an issued patent in China but excluding any Rights in Korea.

We have created a scalable chemical synthetic route for the manufacture of CG-806 drug substance and have been able to scale the manufacture of API (drug substance) to kg levels. We manufactured and delivered a batch of API which was used for Dose Range Finding Studies that were performed and completed in early January 2018. We then completed in March 2018 the manufacture of a multi-kg batch of GLP grade API for use in GLP toxicology studies and have formulated the API into a drug product for use in IND-enabling GLP toxicology studies. We also completed the manufacture of a multi-kg batch of API under GMP conditions that is intended to represent our API supply for our planned first-in-human clinical trials, and we manufactured under GMP conditions two dosage strengths of capsules intended to serve as our clinical supply in planned human studies. Although we have been able to manufacture our API and capsule clinical supplies under GMP conditions, R&D funds are being utilized to support further exploratory formulation studies in an ongoing effort to craft a superior formulation for CG-806. During the year ended December 31, 2018, we completed the in-life dosing phase of the IND-enabling GLP toxicology studies and received audited reports for such studies early in fiscal 2019.

We have increased our patent protection on CG-806. On September 12, 2017, we announced that we received a notice from the USPTO stating that our U.S. Patent Application had been issued as a patent. The patent claims numerous compounds, including the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and methods of treating various diseases caused by abnormal or uncontrolled activation of protein kinases. On July 9, 2018, we received a notice from the Japan Patent Office stating that our Japan Patent Application has been issued as a patent. The patent claims the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and uses for treating various diseases caused by abnormal or uncontrolled activation of protein kinases. On September 27, 2018, we announced that the European Patent Office had issued a patent. The granted patent claims the CG-806 compound, pharmaceutical compositions comprising the CG-806 compound, and uses for treating diseases caused by abnormal or uncontrolled activation of protein kinases, such as cancer. This European patent will be nationalized in, and cover, approximately forty European countries including the United Kingdom, France, Germany, Italy, Netherlands and Spain. The patent is expected to provide protection until the end of 2033.

We have completed several studies that demonstrate the highly differentiated profile of CG-806. Key studies that have been presented at scientific forums are as follows:

- On April 15, 2018 at the 2018 Annual Meeting of the American Association for Cancer Research (AACR), we presented with the OHSU Knight Cancer Institute preclinical data demonstrating that CG-806, a pan-FLT3/pan-BTK inhibitor, demonstrates broader activity and superior potency to other FLT3 and BTK inhibitors against primary bone marrow samples from patients with hematologic malignancies. We also presented preclinical data demonstrating CG-806 targets multiple pathways to kill diverse subtypes of AML and B-cell malignancies in vitro.
- On June 15, 2018 at the 23rd Congress of the European Hematology Association (EHA), we presented, during a poster presentation, preclinical data demonstrating CG-806 unique binding to wild type and C481S mutant BTK. Further, we presented that CG-806 inhibits the BCR, AKT/PI3K, ERK and NFκB signaling pathways and exerts broader and far greater potency than Ibrutinib against malignant bone marrow cells from patients with CLL, ALL and a host of other hematologic malignancies.
- On December 3, 2018, we announced two separate poster presentations at the American Society of Hematology (ASH) Annual Meeting being held on December 1-4, 2018. OHSU Knight Cancer Institute and Aptose presented data in one poster and the team at The University of Texas MD Anderson Cancer Center (MDACC) presented data in a separate poster. These presentations highlighted several key findings. First, in collaboration with the MDACC, orally administered CG-806 demonstrated efficacy in a patient derived xenograft (PDX) study in which the bone marrow cells from a patient with AML having dual ITD and D835 mutations in FLT3 were implanted into a mouse. The dual FLT3 mutant form of AML represents a very difficult to treat population, and the PDX model suggest that CG-806 may be useful in treating such patients. Secondly, Aptose presented high level data from preclinical GLP toxicology studies that demonstrate orally administered CG806 is a well-tolerated targeted molecule. Finally, in collaboration with the OHSU Knight Cancer Center, studies of CG-806 on 124 samples of freshly isolated bone marrow from CLL patients demonstrated both broader and greater cell killing potency for CG-806 than Ibrutinib. Separately, in studies of CG-806 on AML patient bone marrow samples, we identified a previously undiscovered sensitivity in a subpopulation of patients with a particular mutation.
- On February 27, 2019, we announced that new preclinical data will be presented in a poster presentation at the upcoming American Associate for Cancer Research (AACR) being held on March 29-April 3, 2019. Aptose, along with our collaborators at OHSU Knight Cancer Institute will present data highlighting CG-806 was more potent than other FLT3 inhibitors including midostaurin, sorafenib, sunitinib, dovitinib, quizartinib, crenolanib and gilteritinib. CG-806 was equally potent against cells from patients in the adverse, intermediate and favorable risk groups (2017 ELN risk stratification), and cells from patients with relapsed or transformed AML (WHO classification) were as sensitive as those from patients with de novo AML. The data demonstrated potency in primary AML patient samples across all AML subgroups including relapsed/refractory/transformed AML and those with genetic abnormalities related to poor prognosis. While patient samples with FLT3-ITD mutations were expected to have greater sensitivity to CG-806, the most surprising correlation was the sensitivity of patient samples with IDH1 R132 mutations. The enhanced sensitivity of IDH-1 mutant AML to CG-806 warrants investigation in the clinical setting.

CG-806 is being developed with the intent to deliver the agent as an oral therapeutic and to develop it for relapsed and refractory (R/R) AML/high-risk myelodysplastic syndromes (“MDS”) and for appropriate B cell malignancies (including CLL). In collaboration with the FDA, we are finalizing our strategy to perform the clinical studies in patients with AML and B cell malignancies. As clinical trials are lengthy, complex, costly, and uncertain processes, an estimate of the future costs is not reasonable at this time.

On December 26, 2017, we announced that the FDA granted orphan drug designation to CG-806 for the treatment of patients with AML. 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. If CG-806 is approved to treat AML, the orphan drug designation provides us with seven years of marketing exclusivity.

## **APTO-253**

### ***Phase IB Trial***

APTO-253, a small molecule MYC inhibitor, was being evaluated by Aptose in a Phase Ib clinical trial in patients with relapsed / refractory (R/R) hematologic malignancies, particularly R/R-AML and high-risk MDS before being placed on clinical hold by the FDA in November 2015. The Phase Ib trial of APTO-253 was placed on clinical hold as a consequence of an event that occurred at a clinical site with the infusion procedure. Ultimately, a root cause investigation determined that the event resulted from chemistry and manufacturing based issues, all of which were incorporated into a Chemistry, Manufacturing and Control (CMC) amendment to the Investigational New Drug (IND) application. Effective June 29, 2018, the clinical hold was lifted and the APTO-253 clinical trial was re-initiated.



The Phase Ib, multicenter, open-label, dose-escalation clinical trial of APTO-253 is designed to assess the safety, tolerability, pharmacokinetics and pharmacodynamic responses and efficacy of APTO-253 as a single agent and determine the recommended Phase II dose. APTO-253 will be administered once weekly, over a 28-day cycle. The dose escalation stage of the study could potentially enroll up to 20 patients with R/R-AML or high-risk MDS. The study is designed to then transition, as appropriate, to single-agent expansion cohorts in R/R-AML and/or high-risk MDS.

### ***Current Status***

As previously disclosed, the Phase Ib trial was placed on clinical hold in order to solve a chemistry-based formulation issue, and the chemistry of the API and the formulation had undergone minor modifications to deliver a stable and soluble drug product for return to the clinical setting. In December 2016, we had successfully manufactured multiple non-GMP batches of a new drug product formulation for APTO-253; however, a batch that was the intended clinical supply encountered an unanticipated mishap during the filling process that compromised the stability of that batch of drug product. We conducted formal root cause analyses studies, identified the reason for the drug product stability failure, and established a corrective and prevention action plan for the manufacture of future batches of drug product. During the first quarter of 2018, we manufactured a new GMP clinical supply of drug product and performed studies required to demonstrate the fitness of the drug product for clinical usage. The release specifications for the new clinical supply were met, and we presented the findings to the FDA in the second quarter of 2018. On June 28, 2018, the FDA notified us that it had lifted the clinical hold on APTO-253.

We then completed all tasks required to return APTO-253 to the Phase Ib clinical trial. We initiated our first site in September 2018 and in November 2018, we began dosing the first patient. It is important to note 1) only one patient is required for each of the two lowest dose cohorts in this study, 2) that R/R-AML patients are acutely ill, and 3) that a DLT in the first or second cohort could require expansion of the cohort to six patients. For these reasons, Aptose is exercising a highly judicious selection process for patients in the lowest two dose cohorts. This was followed by resubmission of the revised clinical protocol to Institutional Review Boards (IRB) at multiple clinical sites. On November 28, 2018 we announced that we dosed the first patient in the re-initiation of the Phase 1b Clinical Study of APTO-253. In January 2019, we provided data on the Aptose website that we observed meaningful reductions in MYC expression in the PBMC from the first patient dosed with the new formulation of APTO-253.

We are continuing to manufacture additional drug substance and drug product for use in trial. We have completed a second 2kg GMP batch of drug substance and plan shortly to manufacture an additional batch of GMP drug product.

We expect to initiate studies to investigate additional drug delivery methods for APTO-253 and to initiate additional non-clinical studies for solid tumor and hematologic cancer development. As preparing, submitting, and advancing applications for regulatory approval, developing drugs and drug product and clinical trials are sometimes complex, costly, and time-consuming processes, an estimate of the future costs is not reasonable at this time.

Preclinical data presented at scientific forums are as follows:

- On April 17, 2018 at the 2018 Annual Meeting of the American Association for Cancer Research (AACR), we presented preclinical data demonstrating that APTO-253 is a new addition to the repertoire of drugs that can exploit DNA BRCA1/2 deficiency, broadening the potential applicability of APTO-253 towards solid cancer indications.
- On June 4, 2018, we announced that preclinical data elucidating the mechanism of action of APTO-253 were published in two separate articles in the June 2018 issue (Volume 17, Number 6) of Molecular Cancer Therapeutics, a peer-reviewed journal of the American Association for Cancer Research (AACR). The most important finding disclosed in the published articles is the ability of the APTO-253 small molecule to bind to and stabilize a G-quadruplex DNA motif found in the promoter regulatory region of the MYC oncogene and to inhibit expression of the MYC gene, thereby depleting the cells of the MYC oncoprotein and leading to cancer cell death. These findings make APTO-253 the only clinical stage molecule that can directly target the MYC gene and inhibit its expression.
- On February 27, 2019, we announced that new preclinical data will be presented in a poster presentation at the upcoming American Association for Cancer Research (AACR) being held on March 29-April 3, 2019. Aptose, along with our collaborators at the Moores' Cancer Center at UCSD, will present data highlighting APTO-253 activity in down regulation of MYC at mRNA and protein levels, and the mechanisms of drug resistance to APTO-253.

### Multi-Targeting Epigenetic Program

In November 2015, we announced an exclusive drug discovery partnership with Laxai Avanti Life Sciences (“LALS”) for the development of next generation epigenetic-based therapies. Under the agreement, LALS was responsible for optimizing candidates derived from our collaboration with the Moffitt Cancer Center (“Moffitt”), terminated in January 2017, for the development of dual-targeting single agent inhibitors for the treatment of hematologic and solid tumor cancers and we would own global rights to all newly discovered candidates characterized and optimized under the collaboration, including all generated intellectual property. As of November 2016, LALS and we had generated novel compounds that inhibit both the bromodomain proteins and oncogenic kinases, while improving pharmaceutical properties that could serve as a basis for further optimization towards a lead preclinical candidate. However, due to a prioritization of development efforts, LALS and us suspended work on the program in January 2017, and the collaboration with LALS was terminated. However, the program delivered novel intellectual property and compelling hit molecules for further optimization.

On March 7, 2018, we entered into an exclusive global license agreement with Ohm Oncology (OHM), an affiliate of LALS that was formed in 2016 to advance the clinical development of compelling molecules derived from the LALS initiative, for the development, manufacture and commercialization of APL-581, as well as related molecules from our dual bromodomain and extra-terminal domain motif (BET) protein and kinase inhibitor program. Under the agreement, we will retain reacquisition rights to certain molecules, while OHM/LALS will have the rights to develop and sublicense all other molecules. We have received two separate upfront cash payments and are eligible to receive up to \$125 million of additional payments based on the achievement of certain development, regulatory and sales milestones, as well as significant royalties on future sales generated from the program, if any.

### LIQUIDITY AND CAPITAL RESOURCES

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.

The following table presents our cash and cash equivalents, investments and working capital as at December 31, 2018 and December 31, 2017.

(in thousands)	Balances at December 31, 2018	Balances at December 31, 2017
Cash and cash equivalents	\$ 15,299	\$ 10,631
Investments	440	798
Total	\$ 15,739	\$ 11,429
Working capital	\$ 13,697	\$ 10,060

Working capital represents primarily cash, cash equivalents, investments and other current assets less current liabilities.

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. 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 flows:

The following table presents a summary of our cash flows for the years ended December 31, 2018 and 2017:

(in thousands)	For the Years Ended,	
	December 31, 2018	December 31, 2017
Net cash provided by (used in):		
Operating activities	\$ (23,207)	\$ (10,223)
Investing activities	12	(811)
Financing activities	27,871	13,718
Effect of exchange rates changes on cash and cash equivalents	(8)	7
Net increase in cash and cash equivalents	\$ 4,668	\$ 2,691

We are an early stage development company and we currently do not earn any significant 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.

In managing our liquidity risk, we have considered our available cash and cash equivalents and investments as at December 31, 2018. We have also considered our ability to continue to raise funds in 2019 through the ATM Facility with Cantor Fitzgerald and through the 2018 Purchase Agreement with Aspire Capital in assessing whether we will have sufficient resources to fund research and development operations through to at least the twelve-month period ending from the date of this report.

#### ***At-The-Market Facility***

On March 27, 2018, we entered into an at-the-market equity facility (“ATM Facility”) with Cantor Fitzgerald & Co (“Cantor Fitzgerald”), acting as sole agent. Under the terms of this facility, we may, from time to time, sell Common Shares having an aggregate offering value of up to \$30 million through Cantor Fitzgerald. We determine, at our sole discretion, the timing and number of shares to be sold under the ATM Facility.

During the year ended December 31, 2018, we issued 4,085,615 Common Shares under the ATM Facility at an average price of \$2.71 for gross proceeds of approximately \$11.1 million (\$10.7 million net of share issue costs). Subsequent to December 31, 2018, we issued an additional 77,349 Common Shares under this facility at an average price of \$2.37 for gross proceeds of approximately \$183.0 thousand. As at the date of this report, there is approximately \$18.7 million available on this facility.

#### ***Common Shares Purchase Agreements***

In October 2017, we entered into a Common Shares Purchase Agreement (the “Purchase Agreement”) with Aspire Capital Fund, LLC (“Aspire Capital”) to sell up to \$15.5 million of Common Shares to Aspire Capital. Under the terms of the Purchase Agreement, in October 2017, Aspire Capital made an initial purchase of 357,143 Common Shares at a price of \$1.40 per share, representing gross proceeds of approximately \$500.0 thousand (\$324.0 thousand net of share issue costs). During the year ended December 31, 2018, we issued 5,231,953 million Common Shares under the Purchase Agreement at an average price of \$2.77 for gross proceeds of approximately \$15 million. We also issued 321,429 Common Shares at a value of \$1.40 per share to Aspire Capital as consideration for Aspire Capital entering into the Purchase Agreement.

On a cumulative basis, we raised a total of \$15.5 million under the Purchase Agreement, the total amount that was available under the Purchase Agreement.

In May 2018, we entered into a second Common Share Purchase Agreement (the “2018 Purchase Agreement”) with Aspire Capital to sell up to \$20.0 million of Common Shares to Aspire Capital. Under the terms of the 2018 Purchase Agreement, Aspire Capital has committed to purchase up to an aggregate of \$20.0 million of our Common Shares, at our request from time to time during a 30-month period beginning on the effective date of a registration statement related to the transaction and at prices based on the market price at the time of each sale. The registration statement was made effective on June 8, 2018. Under the terms of the 2018 Purchase Agreement, we issued 170,261 Common Shares at a value of \$3.524 per share to Aspire Capital as consideration for Aspire Capital entering into the 2018 Purchase Agreement, and during the year ended December 31, 2018, we issued 907,547 Common Shares at an average price of \$2.12 for gross proceeds of approximately \$1.9 million. Subsequent to December 31, 2018, we issued 3,259,955 shares at an average price of \$1.84 per share for gross proceeds of \$6.0 million. As of the date of this report, there is approximately \$12.0 million available through the 2018 Purchase Agreement.

We will need additional cash in order to execute our research and development plans for our CG-806 and APTO-253 programs and associated general and administrative overhead costs. The Company will use the most efficient source of capital available to it which may include funds available from the ATM Facility and Aspire purchase agreements.

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

At December 31, 2018, we had contractual obligations requiring annual payments as follows:

	Less than 1 year	1 – 3 years	3 – 5 years	Greater than 5 years	Total
Operating leases <sup>(1)</sup>	\$ 419	\$ 938	\$ 607	\$ —	\$ 1,964

(1) Consists primarily of lease obligations for our executive offices in San Diego, California, our Headquarters in Toronto, Ontario, and a research facility located in San Diego, California.

The table above does not include certain general and administrative and development support services under agreements we can cancel without significant penalty.

As at December 31, 2018, we have not entered into any off-balance sheet arrangements other than the operating leases for our offices and labs and certain office equipment.

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.

Under the license agreement with CG, the Company has obligations for development milestones of \$16 million related to the initiation of Phase II 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, we entered into a license agreement with CG to gain an exclusive license to CG-806 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 II 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, 2018 and 2017 is presented below:

(in thousands)	Year ended December 31,	
	2018	2017
Revenues	\$ —	\$ —
Research and development expenses	18,733	6,274
General and administrative expenses	10,374	5,552
Total other income	239	183
Net loss	(28,868)	(11,643)
Other comprehensive loss	—	18
Total comprehensive loss	(28,868)	(11,661)
Basic and diluted loss per common share	(0.86)	(0.52)

Net loss of \$28.9 million for the year ended December 31, 2018 increased by \$17.2 million compared with \$11.6 million for the prior year, primarily as a result of \$5.0 million in license fees paid to CG for development and commercial rights of CG-806, higher research and development expenses related to our CG-806 and APTO- 253 programs, higher professional fees related to regulatory filings in support of financing activities, and from \$4.3 million in non-cash expenses related to stock-based compensation. Excluding the \$5.0 million one-time upfront license fees payments, the net loss for the year ended December 31, 2018 would have been \$23.9 million (\$0.71 per share).

### Research and Development

The research and development expenses for the years ended December 31, 2018 and 2017 are as follows:

(in thousands)	Year ended December 31,	
	2018	2017
License fees – CG-806	\$ 5,000	\$ —
Program costs – CG-806	6,119	2,245
Program costs – APTO-253	4,490	2,328
Personnel expenses	2,063	1,451
Stock-based compensation	1,026	214
Depreciation of equipment	35	36
	18,733	6,274

Research and development expenses of \$18.7 million for the year ended December 31, 2018 increased by \$12.4 million compared with \$6.3 million for the prior year, primarily as a result of the following events:

- License fees paid in the year ended December 31, 2018 to CG of \$2.0 million for development and commercial rights of CG-806 in all territories outside of Korea and China, and a further \$3.0 million paid for development and commercial rights of CG-806 in China. CG is eligible for development, regulatory and commercial-based milestones as well as royalties on future product sales.
- An increase in research and development activities related to our CG-806 development program. In the year ended December 31, 2018, we completed two dose range finding studies and the manufacturing of a batch of the drug substance to be used in toxicity studies, we initiated the manufacturing of a GMP batch of the drug substance for future clinical trials, we completed the manufacturing of GMP batch of drug substance and completed several toxicity studies in rodents and dogs to prepare to bring CG-806 to the clinic. In the comparative periods, activities related to our CG-806 program included mostly formulation and PK studies.
- An increase in expenditures on the APTO-253 program. In the year ended December 31 2018, we completed production of a GMP batch of drug product, we completed necessary studies required for the FDA, we initiated the manufacturing of an additional clinical batch of APTO-253, we increased clinical activities in preparation to return APTO-253 to the clinic, we manufactured additional API, and initiated three clinical sites and began dosing our first patient. In the comparative periods, we were conducting root cause analysis to determine the cause of a manufacturing issue that had resulted in the program being on clinical hold.
- An increase in personnel expense mostly related to additional clinical research staff hired to prepare for returning APTO-253 to the clinic and to preparing CG-806 for clinical studies.
- An increase in stock-based compensation related mostly to approximately 462 thousand stock options granted to clinical operations and research employees in the three months ended March 31, 2018, of which 100,000 with a grant date fair value of \$2.03 per share vested immediately. In addition, stock-based compensation is also higher because of 50,000 restricted share units issued in July 2018 with a three-month vesting term and a grant date fair value of \$3.35 per share.

#### **General and Administrative**

The general and administrative expenses for the years ended December 31, 2018 and 2017 are as follows:

(in thousands)	Year ended December 31,	
	2018	2017
General and administrative, excluding non-cash items	\$ 6,471	\$ 4,900
Shares issued pursuant to Aspire 2018 Purchase Agreement	600	—
Stock-based compensation	3,250	602
Depreciation of equipment	53	50
	<u>10,374</u>	<u>5,552</u>

General and administrative expenses of \$10.4 million for the year ended December 31, 2018 increased by \$4.8 million compared with \$5.6 million for the prior year, primarily as a result of the following:

General and administrative expenses, excluding non-cash items, increased primarily as a result of higher professional fees related to regulatory filings in support of financing activities, higher investor relations costs, higher patent fees associated with our expanded IP portfolio, and higher office administrative costs associated with additional employees to support increased operations of the Company.

In June 2018, we issued 170,261 shares to Aspire Capital as a commitment fee for entering into the 2018 Purchase Agreement, as further described above under “Liquidity and Capital Resources, Common Shares Purchase Agreements.” We recorded \$600 thousand in general and administrative expenses related to the issuance of these shares.

Stock-based compensation increased in the year ended December 31, 2018, compared with the year ended December 31, 2017 mostly related to approximately 1.6 million stock options granted to directors, executive officers and general and administrative employees in the three-month period ended March 31, 2018, of which 750,000 with a grant date fair value of \$2.03 vested immediately, and also as a result of large forfeitures in the three months ended March 31, 2017. In addition, stock-based compensation is also higher in the current period related to 100,000 restricted share units issued to executive officers in July 2018 with a three-month vesting term and a grant date fair value of \$3.35.

## **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 of Directors 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 valuation of contingent liabilities, the valuation of tax accounts, and the assumptions used in determining the valuation of share-based compensation.

### ***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, 2018 and 2017, respectively, are presented in Note 8 to the consolidated financial statements.

### ***Leases***

In February 2016, the FASB issued ASU No. 2016-02, "Leases (Topic 842)", or ASU No. 2016-02. Under the new guidance, lessees will be required to recognize a right-of-use asset, 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. ASU No. 2016-02 is effective beginning January 1, 2019 and early adoption is permitted. ASU No. 2016-02 must be adopted on a modified retrospective transition basis at the beginning of the earliest comparative period presented in the consolidated financial statements or at the adoption date. The adoption of ASU No. 2016-02 will result in a significant increase in our consolidated balance sheet for right-of-use assets and a corresponding increase to lease liabilities related to leases of our facilities. The future minimum lease payments under these leases at December 31, 2018 were approximately \$2.0 million. In addition, we will de-recognize existing leasehold improvements and accruals for lease incentives upon the adoption of ASU No. 2016-02.

### ***Updated share information***

As at March 12, 2019, we had 41,499,112 Common Shares issued and outstanding. In addition, there were 5,685,242 Common Shares issuable upon the exercise of outstanding stock options and upon the vesting of restricted share units.

### **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 required by this item are included in the Exhibits to 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**

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, 2018, 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, 2018, our internal control over financial reporting was effective based on those criteria. We are an "emerging growth company," as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act.

### **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, 2018, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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

None.

### **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 2019 Annual Meeting of Shareholders, referred to as the Proxy Statement, which will be filed with the SEC within 120 days of the 2018 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,” “Corporate Governance – Board Committees” and “Section 16(a) Beneficial Ownership Reporting Compliance,” 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:

[Report of Independent Registered Public Accounting Firm](#)  
[Balance Sheets](#)  
[Statements of Operations and Comprehensive Loss](#)  
[Statements of Shareholders' Equity](#)  
[Statements of Cash Flows](#)  
[Notes to Financial Statements](#)

Page
<a href="#">F-1</a>
<a href="#">F-3</a>
<a href="#">F-4</a>
<a href="#">F-5</a>
<a href="#">F-6</a>
<a href="#">F-7</a>

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

The following exhibits are filed as part of, or incorporated by reference into, this report:

Exhibit Number	Description of Document
<a href="#">3.1</a>	<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>
<a href="#">3.2</a>	<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>
<a href="#">4.1</a>	<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>
<a href="#">4.2</a>	<a href="#">Registration Rights Agreement dated October 27, 2017 by and between the Company and Aspire Capital Fund, LLC (incorporated herein by reference to Exhibit 99.2 to the Company's Current Report on Form 6-K filed with the SEC filed on October 30, 2018)</a>
<a href="#">4.3</a>	<a href="#">Registration Rights Agreement dated May 30, 2018 by and between the Company and Aspire Capital Fund, LLC (incorporated herein by reference to Exhibit 99.2 to the Company's Current Report on Form 6-K filed with the SEC filed on May 31, 2018)</a>
<a href="#">10.1</a>	<a href="#">Common Share Purchase Agreement dated May 30, 2018 by and between the Company and Aspire Capital Fund, LLC (incorporated herein by reference to Exhibit 99.1 to the Company's Current Report on Form 6-K filed with the SEC filed on May 31, 2018)</a>
<a href="#">10.2</a>	<a href="#">Controlled Equity Offering<sup>SM</sup> Sales Agreement dated March 27, 2018 by and between the Company and Cantor Fitzgerald &amp; Co. (incorporated herein by reference to Exhibit 99.1 to the Company's Current Report on Form 6-K filed with the SEC filed on March 28, 2018)</a>
<a href="#">10.3</a>	<a href="#">Common Shares Purchase Agreement dated October 27, 2017 by and between the Company and Aspire Capital Fund, LLC (incorporated herein by reference to Exhibit 99.1 to the Company's Current Report on Form 6-K filed with the SEC filed on October 30, 2017)</a>
<a href="#">10.4</a>	<a href="#">Sales Agreement dated April 2, 2015 by and between the Company and Cowen and Company, LLC (incorporated herein by reference to Exhibit 1.1 to the Company's Current Report on Form 6-K filed with the SEC filed on April 6, 2015)</a>
<a href="#">10.5+</a>	<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>

Exhibit Number	Description of Document
<a href="#">10.6+</a>	<a href="#">Executive Employment Agreement between the Company and Gregory K. Chow dated November 29, 2013 (incorporated herein by reference to Exhibit 4.9.1 to the Company's Annual Report on Form 20-F filed with the SEC on May 16, 2014)</a>
<a href="#">10.7+</a>	<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>
<a href="#">10.8+</a>	<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>
<a href="#">10.9^^</a>	<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>
<a href="#">10.10^</a>	<a href="#">Option and License Agreement between the Company and CrystalGenomics, Inc., dated March 21, 2016 (incorporated herein by reference to Exhibit 99.1 to the Company's Current Report on Form 6-K filed with the SEC on June 8, 2016)</a>
<a href="#">10.11</a>	<a href="#">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)</a>
<a href="#">10.12</a>	<a href="#">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)</a>
<a href="#">10.13</a>	<a href="#">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)</a>
<a href="#">10.14</a>	<a href="#">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)</a>
<a href="#">10.15^</a>	<a href="#">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)</a>
<a href="#">21.1</a>	<a href="#">List of subsidiaries</a>
<a href="#">23.1*</a>	<a href="#">Consent of Independent Registered Accounting Firm (KPMG LLP)</a>
<a href="#">24.1*</a>	<a href="#">Powers of Attorney (included on signature page)</a>
<a href="#">31.1*</a>	<a href="#">Certification of Principal Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>
<a href="#">31.2*</a>	<a href="#">Certification of Principal Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>
<a href="#">32.1*</a>	<a href="#">Certification of Principal Executive Officer Pursuant Section 906 of the Sarbanes-Oxley Act of 2002.</a>
<a href="#">32.2*</a>	<a href="#">Certification of Principal Financial Officer Pursuant Section 906 of the Sarbanes-Oxley Act of 2002.</a>
<a href="#">101**</a>	The following financial statements from the Aptose Biosciences Inc. Annual Report on Form 10-K for the years ended December 31, 2018, 2017 and 2016, formatted in Extensible Business Reporting Language (XBRL): (i) statements of operations and comprehensive loss, (ii) balance sheets, (iii) statements of shareholders' equity, (iv) statements of cash flows, and (v) the notes to the financial statements.
+	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 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 12th day of March, 2019.

Aptose Biosciences Inc.

/s/ William G. Rice

By:

\_\_\_\_\_  
William G. Rice  
Chairman, Chief Executive Officer and  
President

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Dr. William G. Rice and Mr. Gregory K. Chow, 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.

<b>Signature</b>	<b>Title</b>
<u>/s/ William G. Rice</u> William G. Rice	President, Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer)
<u>/s/ Gregory K. Chow</u> Gregory K. Chow	Senior Vice President and Chief Financial Officer (Principal Financial Officer and Accounting Officer)
<u>/s/ Denis R. Burger</u> Denis R. Burger	Director, Lead Independent
<u>/s/ Carol G. Ashe</u> Carol G. Ashe	Director
<u>/s/ Caroline Loewy</u> Caroline Loewy	Director
<u>/s/ Erich M. Platzer</u> Erich M. Platzer	Director
<u>/s/ Mark D. Vincent</u> Mark D. Vincent	Director
<u>/s/ Warren Whitehead</u> Warren Whitehead	Director



Consolidated Financial Statements of

**APTOSE BIOSCIENCES INC.**

Years ended December 31, 2018 and 2017

---



## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Aptose Biosciences Inc.

### *Opinion on the Financial Statements*

We have audited the accompanying consolidated statements of financial position of Aptose Biosciences Inc. (the "Company") as of December 31, 2018 and December 31, 2017, 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 referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and December 31, 2017, and its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

### *Change in Accounting Framework and Principle*

Without qualifying our opinion on the financial statements, we draw attention to Note 2b to the financial statements, which indicates that the Company has retrospectively adopted United States generally accepted accounting principles (U.S. GAAP). Comparative figures, which were previously presented in accordance with International Financial Reporting Standards as issued by the International Accounting Standards Board, have been adjusted as necessary.

Without qualifying our opinion on the financial statements, we draw attention to Note 2b to the financial statements, which indicates that the Company has changed its functional and presentation currency from Canadian dollar to US dollar. The change in functional currency is as of January 1, 2017. The change in presentation currency is as of December 31, 2017, and this change has been retrospectively applied in the financial statements.

### *Basis for Opinion*

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's 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 and in accordance with the ethical requirements that are relevant to our audit of the financial statements in Canada.

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 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 purposes 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 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 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 financial statements. We believe that our audits provide a reasonable basis for our opinion.



We have served as the Company's auditor since 2003.

*KPMG LLP*

Chartered Professional Accountants, Licensed Public Accountants  
Vaughan, Canada  
March 12, 2019

**APTOSE BIOSCIENCES INC.**Consolidated Statements of Financial Position  
(Expressed in thousands of US dollars)

	December 31, 2018	December 31, 2017
		(notes 2(a) and 15)
<b>Assets</b>		
<b>Current assets:</b>		
Cash and cash equivalents	\$ 15,299	\$ 10,631
Investments	440	798
Prepaid expenses	646	322
Other current assets	101	74
<b>Total current assets</b>	<b>16,486</b>	<b>11,825</b>
<b>Non-current assets:</b>		
Property and equipment	384	142
<b>Total non-current assets</b>	<b>384</b>	<b>142</b>
<b>Total assets</b>	<b>\$ 16,870</b>	<b>\$ 11,967</b>
<b>Liabilities and Shareholders' Equity</b>		
<b>Current liabilities:</b>		
Accounts payable	\$ 1,315	\$ 589
Accrued liabilities	1,474	1,176
<b>Total current liabilities</b>	<b>2,789</b>	<b>1,765</b>
<b>Commitments (note 12)</b>		
<b>Shareholders' equity:</b>		
<b>Share capital:</b>		
Common shares, no par value, unlimited authorized shares, 38,161,808 and 27,502,053 shares issued and outstanding at December 31, 2018 and December 31, 2017	261,072	231,923
Additional paid-in capital	32,963	29,365
Accumulated other comprehensive loss	(4,316)	(4,316)
Deficit	(275,638)	(246,770)
<b>Total shareholders' equity</b>	<b>14,081</b>	<b>10,202</b>
<b>Total liabilities and shareholders' equity</b>	<b>\$ 16,870</b>	<b>\$ 11,967</b>

See accompanying notes to consolidated financial statements.

*Subsequent events (note 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, 2018	Year ended December 31, 2017 (notes 2(a) and 15)
Revenue	\$ -	\$ -
Expenses:		
Research and development	18,733	6,274
General and administrative	10,374	5,552
Operating Expenses	29,107	11,826
Other income (expense):		
Interest income	283	68
Foreign exchange gains( losses)	(44)	115
Total other income	239	183
Net loss	(28,868)	(11,643)
Other comprehensive loss:		
Unrealized loss on securities available-for-sale	-	18
Total comprehensive loss	\$ (28,868)	\$ (11,661)
Basic and diluted loss per common share	\$ (0.86)	\$ (0.52)
Weighted average number of common shares outstanding used in the calculation of (in thousands) Basic and diluted loss per common share	33,391	22,313

See accompanying notes to consolidated financial statements



**APTOSE BIOSCIENCES INC.**

## Consolidated Statements of Changes in Shareholders' Equity

(notes 2(a) and 15)

(Expressed in thousands of US dollars)

	Common Shares		Additional paid-in capital	Accumulated other comprehensive loss	Deficit	Total
	Shares	Amount				
Balance, December 31, 2017	27,502	\$ 231,923	\$ 29,365	\$ (4,316)	\$ (246,770)	\$ 10,202
Common shares issued under the 2018 ATM	4,086	10,710	-	-	-	10,710
Common shares issued pursuant to 2017 purchase agreement	5,232	14,995	-	-	-	14,995
Common shares issued pursuant to 2018 purchase agreement	1,078	2,526	-	-	-	2,526
Shares issued on redemption of restricted share units	150	503	(503)	-	-	-
Common shares issued upon exercise of stock options	114	415	(175)	-	-	240
Stock-based compensation	-	-	4,276	-	-	4,276
Net loss	-	-	-	-	(28,868)	(28,868)
Balance, December 31, 2018	38,162	\$ 261,072	\$ 32,963	\$ (4,316)	\$ (275,638)	\$ 14,081
Balance, December 31, 2016	15,722	\$ 218,034	\$ 28,719	\$ (4,298)	\$ (235,127)	\$ 7,328
Common shares issued under the ATM	10,952	13,394	-	-	-	13,394
Common shares issued pursuant to purchase agreement	978	324	-	-	-	324
Shares issued on redemption of restricted share units	150	171	(171)	-	-	-
Stock-based compensation	-	-	817	-	-	817
Other comprehensive loss	-	-	-	(18)	-	(18)
Net loss	-	-	-	-	(11,643)	(11,643)
Balance, December 31, 2017	27,502	\$ 231,923	\$ 29,365	\$ (4,316)	\$ (246,770)	\$ 10,202

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, 2018	Year ended December 31, 2017 (notes 2(a) and 15)
<b>Cash flows from operating activities:</b>		
Net loss for the year	\$ (28,868)	\$ (11,643)
<b>Items not involving cash:</b>		
Stock-based compensation	4,276	817
Shares issued to Aspire Capital as commitment fees	600	-
Depreciation and amortization	87	84
Unrealized foreign exchange loss	25	(25)
<b>Change in non-cash operating working capital:</b>		
Prepaid expenses	(324)	70
Other assets	(27)	27
Accounts payable	726	589
Accrued liabilities	298	(142)
Cash used in operating activities	(23,207)	(10,223)
<b>Cash flows from financing activities:</b>		
Issuance of common shares under the 2018 ATM, net of broker commission	10,720	-
Issuance of common shares under the ATM, net of broker commission	-	13,525
Issuance of common shares under 2018 share purchase agreement	1,926	-
Issuance of common shares under 2017 share purchase agreement	15,000	500
Offering costs paid	(15)	(307)
Exercise of stock options	240	-
Cash provided by financing activities	27,871	13,718
<b>Cash flows from (used in) investing activities:</b>		
Maturity (acquisition) of investments, net	341	(798)
Purchase of property and equipment	(329)	(13)
Cash provided by (used in) investing activities	12	(811)
Effect of exchange rate fluctuations on cash and cash equivalents held	(8)	7
Increase in cash and cash equivalents	4,668	2,691
Cash and cash equivalents, beginning of year	10,631	7,940
Cash and cash equivalents, end of year	\$ 15,299	\$ 10,631

See accompanying notes to consolidated financial statements

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

---

**1. Reporting entity:**

Aptose Biosciences Inc. (“Aptose” or the “Company”) is a clinical-stage biotechnology company committed to discovering and developing personalized therapies addressing unmet medical needs in oncology. The Company’s executive offices are located in San Diego, California and its head office is located in Toronto, Canada.

Aptose has one clinical-stage program, one IND-stage program, and a third program that is discovery-stage and partnered with another company. CG026806 (“CG-806”), Aptose’s pan- FMS-like tyrosine kinase 3 / pan-Bruton’s tyrosine kinase inhibitor, is currently at the IND submission stage of development (we submitted the investigational new drug (“IND”) application to the U.S. Food and Drug Administration (FDA) in February 2019. Development of CG-806 is intended for the treatment of patients with relapsed / refractory Acute Myeloid Leukemia (R/R AML) and patients having certain B-cell malignancies. APTO-253, Aptose’s second program, is a small molecule MYC inhibitor and is currently enrolling patients in a Phase 1b clinical trial for the treatment of patients with R/R blood cancers, including AML and high-risk Myelodysplastic Syndrome.

**2. Significant accounting policies**

(a) Adoption of US GAAP:

The Company’s consolidated financial statements have been prepared by management in accordance with United States generally accepted accounting principles (U.S. GAAP). Comparative figures, which were previously presented in accordance with International Financial Reporting Standards (“IFRS”) as issued by the International Accounting Standards Board have been adjusted as necessary to be compliant with the Company’s policies under U.S. GAAP and are further described in note 15.

(b) Basis of presentation:

These consolidated financial statements of Aptose Biosciences Inc., which include the accounts of its subsidiaries have been prepared in accordance with U.S. generally accepted accounting principles, or U.S GAAP. All intercompany transactions, balances, revenue and expenses are eliminated on consolidation

(c) Significant accounting policies, estimates and judgments:

The preparation of these 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 include 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) Foreign currency:

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

Effective January 1, 2017, the Company changed its functional currency to US dollars given the prevalence of US dollar denominated activities over time. Since the Company’s inception in 1986 to fiscal 2014 all operations of the entity were conducted in Canada and the Canadian dollar was determined to be the functional currency. During fiscal years 2015 and 2016, the Company gradually transitioned most of its research and development activities, including both headcount and studies, to the US, and completed this transition in January 2017.

(e) Cash and cash equivalents:

Cash and cash equivalents are short-term highly liquid investments with original maturities of three months or less as at the date of purchase.

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

**(f) Investments:**

Investments consist of time deposits with original maturities greater than three months are classified by management as securities available-for-sale. These available-for-sale 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 Canadian corporations which are capable of prompt liquidation.

**(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 (years)	5
Laboratory equipment (years)	5
Computer hardware (years)	3
Computer software (years)	3
Leasehold improvements	Life of lease

The assets' residual value, useful life and methods of depreciation 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, intangibles, 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.

**(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 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.

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

---

Stock options awarded to non-employees are accounted for at the fair value of the goods received or the services rendered. The fair value is measured at the grant date. In June 2018, FASB issued accounting standards update No 2018-07, Improvements to Nonemployee Share-Based Payment Accounting. The amendment establishes that nonemployee share-based payment awards within the scope of Topic 718 be measured at grant-date fair value of the equity instruments issued. The amendments are effective for fiscal years beginning after December 15, 2018. Early adoption is permitted and the Company elected to early adopt this policy upon its conversion to US GAAP. The early adoption did not result in any changes in retained earnings or other components of equity as the accounting.

The Company has a stock incentive plan pursuant to which the Board may grant 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 shares 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 at December 31, 2017 and December 31, 2017, 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) Recently issued accounting pronouncements not yet adopted

In February 2016, the FASB issued ASU No. 2016-02, "Leases (Topic 842)", or ASU No. 2016-02. Under the new guidance, lessees will be required to recognize a right-of-use asset, 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. ASU 2016-02 is effective for reporting periods beginning after December 15, 2018 and requires either a modified retrospective transition approach with application in all comparative periods presented, or an alternative transition method, which permits a company to use its effective date as the date of initial application without restating comparative period financial statements. Early adoption is permitted. We plan to adopt this standard in the first quarter of the fiscal year ending December 31, 2019 using the alternative transition method with the effective date as of January 1, 2019. We are in the process of finalizing the impact that this new standard will have on our financial statements and disclosures. The adoption of ASU No. 2016-02 will result in a significant increase in our consolidated balance sheet for right-of-use assets and a corresponding increase to lease liabilities related to leases of our facilities. The future minimum lease payments under these leases at December 31, 2018 were approximately \$2.0 million. In addition, we will de-recognize existing leasehold improvements and accruals for lease incentives upon the adoption of ASU No. 2016-02.

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

**3. Cash and cash equivalents:**

Cash and cash equivalents consists of cash of \$621 thousand (December 31, 2017 - \$3.225 million), deposits in high interest savings accounts and other term deposits with maturities less than 90 days totaling \$14.678 million (December 31, 2017 - \$7.406 million).

**4. Property and equipment:**

December 31, 2018	Cost	Accumulated depreciation	Net book value
Laboratory equipment	\$ 176	\$ 129	\$ 47
Computer hardware	80	40	40
Computer software	222	80	142
Office furniture	82	28	54
Leasehold improvements	160	59	101
	\$ 720	\$ 336	\$ 384

December 31, 2017	Cost	Accumulated depreciation	Net book Value
Laboratory equipment	\$ 173	\$ 94	\$ 79
Computer hardware	47	31	16
Computer software	80	79	1
Office furniture	35	19	16
Leasehold improvements	69	39	30
	\$ 404	\$ 262	\$ 142

**5. Investments:**

Investments consisted of the following as of December 31, 2018 and 2017:

December 31, 2018			
	Cost	Unrealized loss	Market value
Guaranteed investment certificate	\$ 458	(18)	440

December 31, 2017			
	Cost	Unrealized loss	Market value
Guaranteed investment certificate	\$ 816	(18)	798

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

**6. 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 company's assets that are measured at fair value on a recurring basis for the periods presented:

	December 31		Level 1	Level 2	Level 3
	2018				
<b>Assets</b>					
High interest savings account	\$	496	\$ -	\$ 496	-
United States treasury bills		3,989	-	3,989	-
Canadian provincial promissory notes		5,991	-	5,991	-
Guaranteed investment certificates, Royal Bank of Canada		4,642	-	4,642	-
	\$	15,118	\$ -	\$ 15,118	\$ -
	December 31		Level 1	Level 2	Level 3
	2017				
<b>Assets</b>					
Canadian provincial promissory notes		2,003	-	2,003	-
Commercial Notes		1,999	-	1,999	-
Guaranteed income certificates, Royal Bank of Canada		4,202	-	4,202	-
		8,204	\$ -	\$ 8,204	\$ -

**7. Accrued liabilities:**

Accrued liabilities as of December 31, 2018 and 2017 consisted of the following (in thousands):

	December 31,	
	2018	2017
Accrued personnel related costs	\$ 955	\$ 734
Accrued research and development expenses	257	176
Other accrued expenses	262	266
	\$ 1,474	\$ 1,176

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

---

**8. Share capital:**

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

(a) Equity issuances:

(i) 2018 At-The-Market (“ATM”) Facility

On March 28, 2018, the Company entered into an “At-The-Market” Facility (“ATM”) equity distribution agreement with Cantor Fitzgerald acting as sole agent. Under the terms of this facility, the Company may, from time to time, sell shares of our common stock having an aggregate offering value of up to \$30 million through Cantor Fitzgerald on the Nasdaq Capital Market. During the year ended December 31, 2018, the Company issued 4,085,615 shares under this ATM equity facility at an average price of \$2.71 for gross proceeds of \$11 million (\$10.7 million net of share issue costs). Costs associated with the proceeds consisted of a 3% cash commission.

(ii) 2017 Share purchase agreement

On October 27, 2017, we entered into the 2017 Aspire Purchase Agreement, which provided that, upon the terms and subject to the conditions and limitations set forth therein, Aspire Capital is committed to purchase up to an aggregate of \$15,500,000 of Common Shares over approximately 30 months. During the year ended December 31, 2017 and pursuant to the terms of the Aspire Purchase Agreement, Aspire Capital purchased 357,143 Common Shares for gross proceeds of \$500 thousand (\$324 thousand net of cash share issue costs) and we also issued 321,429 Common Shares to Aspire Capital in consideration for entering into the Aspire Purchase Agreement. During the year ended December 31, 2018, the Company issued 5,231,953 common shares under the Aspire Purchase Agreement at an average price of \$2.87 per share for gross and net proceeds of approximately \$15 million. On a cumulative basis to December 31, 2018, the Company has raised a total of \$15.5 million gross proceeds under the Aspire Purchase Agreement, the total amount that was available under the Agreement.

(iii) 2018 Share Purchase Agreement

On May 30, 2018, the Company entered into the 2018 Aspire Purchase Agreement, which provides that, upon the terms and subject to the conditions and limitations set forth therein, Aspire Capital is committed to purchase up to an aggregate of \$20 million of Common Shares over approximately 30 months. Pursuant to the terms of this agreement, on June 8, 2018, the Company issued 170,261 Common Shares (“Commitment Shares”) to Aspire Capital in consideration for entering into the 2018 Aspire Purchase Agreement. The Company recorded \$600 thousand in general and administrative expenses related to the issuance of the Commitment Shares. During the year ended December 31, 2018, the Company issued 907,547 shares under the 2018 Aspire Purchase Agreement at an average price of \$2.12 per share for gross and net proceeds of approximately \$1.9 million.

(iv) At-The-Market (“ATM”) Facility

On April 2, 2015, Aptose entered into an at-the-market (“ATM”) equity facility with Cowen and Company, LLC, acting as sole agent. Under the terms of the ATM, Aptose was permitted to sell Common Shares having an aggregate offering value of US\$20,000,000 on NASDAQ. During the year ended December 31, 2017, the Company issued 10,952,093 common shares under the ATM at an average price of \$1.27 per share for gross proceeds of \$13.9 million (\$13.4 million net of share issue costs). Costs associated with the proceeds included a 3% cash commission. The ATM expired on December 29, 2017 and as at that date the Company had issued a cumulative \$20,000,000 of Common Shares pursuant to this facility.



**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

## (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 Dec 31, 2018	Year ended Dec 31, 2017
Net loss	\$ (28,868)	\$ (11,643)
Weighted-average common shares – basic and diluted	33,391	22,313
Net loss per share – basic and diluted	\$ (0.86)	\$ (0.52)

The effect of any potential exercise of the Company's stock options outstanding during the year has been excluded from the calculation of diluted loss per common share as it would be anti-dilutive.

**9. Stock-based compensation:**

## (a) Stock options

Under the Company's stock option plan, options, rights and other entitlements may be granted to directors, officers, employees and consultants of the Company to purchase up to a maximum of 17.5% of the total number of outstanding common shares, estimated at 6.7 million options, rights and other entitlements as at December 31, 2018. Options are granted at the fair market value of the common shares on 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. Options vest at various rates (immediate to four years) and have a term of 10 years.

Stock option transactions for the years ended December 31, 2017 and 2018 are summarized as follows:

*Option numbers are in (000's)*

	Options	Year ended December 31, 2018 Weighted average exercise price	Weighted average remaining contractual life (years)	Aggregate Intrinsic Value
Outstanding, January 1, 2017	2,005	\$ 4.31		
Granted	826	1.19		
Expired	(323)	4.58		
Forfeited	(164)	3.35		
Outstanding, December 31, 2017	2,344	\$ 3.46		
Granted	2,320	2.98		
Exercised	(114)	2.04		
Expired	(51)	2.34		
Forfeited	(10)	4.97		
Outstanding, December 31, 2018	4,489	\$ 3.11	7.9	\$ 562,438
Exercisable, December 31, 2018	2,544	\$ 3.41	7.1	273,907
Vested and expected to vest, December 31, 2108	4,196	\$ 3.06	7.8	519,159

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 \$255 thousand for the year ended December 31, 2018, and nil for 2017.

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

As of December 31, 2018, there was \$1.28 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 1.83 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 year, and the resultant weighted average fair values:

	Year ended December 31, 2018	Year ended December 31, 2017
Risk-free interest rate	2.43%	1.32%
Expected dividend yield	-	-
Expected volatility	93.3%	98%
Expected life of options (years)	5	5
Grant date fair value	\$ 2.22	\$ 0.87

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.

Stock options granted by the Company during the twelve months ended December 31, 2018 vest 50% after one year and 16.67% on each of the next three anniversaries, except for 166,000 options which vest 50% after one year and 25% on each of the next two anniversaries and 850,000 options which vested immediately on the grant date.

Stock options granted by the Company during the year ended December 31, 2017 consist of 641,500 options that vest 50% after one year and 16.67% on each of the next three anniversaries, and 185,000 options that vest 50% after one year and 25% on each of the next two anniversaries.

**(b) Restricted share units**

The Company has a stock incentive plan (SIP) pursuant to which the Board may grant 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. Each restricted unit is automatically redeemed for one common share of the Company upon vesting. The following table presents the activity under the SIP plan for the years ended December 31, 2018 the units outstanding.

	Year ended, December 31, 2018		Year ended, December 31, 2017	
	Number (in thousands)	Weighted average grant date fair value	Number (in thousands)	Weighted average grant date fair value
Outstanding, beginning of period	-	\$-	-	\$-
Granted	150	3.35	150	1.14
Redeemed	(150)	3.35	(150)	1.14
Outstanding, end of period	-	\$ -	-	\$ -

On March 28, 2017 the Company granted 150,000 restricted share units (RSUs) with a vesting term of three months. On July 13, 2018, the Company granted 150,000 restricted share units with a vesting term of three months. During the three-month and twelve-month period ending December 31, 2018, the Company recorded share-based payment expense of approximately \$66 thousand (2017- nil) and \$503 thousand (2017 - \$171 thousand), respectively, related to the issued RSUs.

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

The grant date fair value of the July 13, 2018 RSUS was determined as the closing value of the common shares of the Company on the Nasdaq Stock Exchange on the date prior to the date of grant; and for March 28, 2017 RSUs, the grant date fair value was determined as the closing value of the common shares of the Company on the Toronto Stock Exchange on the date prior to the date of grant.

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

	Year ended December 31, 2018	Year ended December 31, 2017
Research and development	\$ 1,026	\$ 214
General and administrative	3,250	603
<b>Total</b>	<b>\$ 4,276</b>	<b>\$ 817</b>

**10. Related party transactions:**

The Company uses Moores Cancer Center at the University of California San Diego (UCSD) to provide pharmacology lab services to the Company. Dr. Stephen Howell is the Acting Chief Medical Officer of Aptose and is also a Professor of Medicine at UCSD and oversees the laboratory work. The work is completed under the terms of research services agreements executed in March 2015 and has been extended annually. In March 2018, the Board approved an extension of this agreement for twelve months for services up to \$300,000. These transactions are in the normal course of business and are measured at the amount of consideration established and agreed to by the related parties.

During year ended December 31, 2018, the Company recorded \$279 thousand (2017 – \$240 thousand) in research and development expenses related to the agreement.

**11. 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.

Under the Company's license agreement with CrystalGenomics for rights to CG-806, 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 CG-806 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.

On March 7, 2018, we entered into an exclusive global license agreement with Ohm Oncology (OHM), for the development, manufacture and commercialization of APL-581, as well as related molecules from our dual bromodomain and extra-terminal domain motif (BET) protein and kinase inhibitor program. Under the agreement, we will retain reacquisition rights to certain molecules, while OHM/LALS will have the rights to develop and sublicense all other molecules. We have received two nominal upfront cash payments and are eligible to receive up to \$125 million of additional payments based on the achievement of certain development, regulatory and sales milestones, as well as significant royalties on future sales generated from the program, if any.

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

**12. Commitments**

Operating lease commitments:

As at December 31, 2018, the Company has entered into operating leases for premises and equipment under which it is obligated to make minimum annual payments as described below:

Years ending December 31,	
2019	\$ 419
2020	464
2021	474
2022	478
2023	129
Thereafter	-
	\$ 1,964

Lease expense under our operating leases was as follows:

	Year ended December 31, 2018	Year ended December 31, 2017
Lease expense	\$ 354	\$ 329

**13. Income taxes:**

## a) Recent tax legislation

In December 2017 the U.S. government enacted comprehensive tax legislation, the Tax Cuts and Jobs Act (the "Tax Act"), which significantly revises the U.S. tax code, generally effective January 1, 2018, by lowering the U.S. federal corporate income tax rate from 35% to 21%, implementing a territorial tax system and setting limitations on the deductibility of certain costs (e.g. Interest expenses) among other things. As a Canadian entity, we generally would be classified as a foreign entity (and, therefore, a non-U.S. tax resident) under general rules of U.S. federal income taxation. However, we have a branch and U.S. subsidiary subject to U.S. federal income taxation. The Tax Act has impacted our consolidated results of operations during 2017 and 2018, and is expected to continue to impact our consolidated results of operations in future periods. The ultimate impact of the Tax Act on our effective tax rate in future periods will depend on interpretations and regulatory changes from the Internal Revenue

## b) Income taxes

For the years ended December 31, 2017 and 2018, the total comprehensive loss is as follows:

	December 31, 2018	December 31, 2017
Loss attributed to US foreign operations	\$ (21,807)	\$ (7,805)
Loss losses not attributed to Canadian operations	(7,061)	(3,856)
Income (loss) before income taxes	(28,868)	(11,661)

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

## c) Tax rate reconciliation

Major items causing the Company's income tax rate to differ from the statutory rate of approximately 26.5% (December 31, 2017 – 26.5%) are as follows:

	Year ended December 31, 2018	Year ended December 31, 2017
Net loss	\$ (28,868)	\$ (11,661)
Statutory Canadian corporate tax rate	26.5%	26.5%
Computed "expected" tax recovery	\$ (7,650)	\$ (3,090)
Non-deductible permanent differences	1,422	220
Change in valuation allowance	4,528	4,619
Foreign tax rate differential	(325)	(117)
Change in enacted rates	-	51
Foreign exchange differences	2,183	(1,391)
Other	(158)	(292)
	\$ -	\$ -

## d) 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, 2018	December 31, 2017
Net operating losses carried forward	\$ 19,567	\$ 15,762
Research and development expenditures	5,024	5,450
Intangible asset	3,531	2,464
Equipment book over tax depreciation	367	410
Ontario Research and Development Tax Credit	394	427
Undeducted financing costs	452	273
Cumulative eligible capital	263	284
Total deferred tax assets	29,598	25,070
Valuation allowance	(29,598)	(25,070)
Net deferred tax asset	\$ -	\$ -

The valuation allowance at December 31, 2018 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 undeducted research and development expenditures, totaling \$18.95million that can be carried forward indefinitely. The Company also has Canadian non-refundable federal investment tax credits of approximately \$3.95 million which are available to reduce future federal taxes payable and begin to expire in 2019, as well as non-refundable Ontario research and development tax credits of approximately \$393 thousand which are available to reduce future Ontario taxes payable and begin to expire in 2028.

In addition, the Company has non-capital loss carryforwards of \$72 million. To the extent that the non-capital loss carryforwards are not used, they begin to expire in 2026.

**APTOSE BIOSCIENCES INC.**

Notes to Consolidated Financial Statements

(Tabular amounts in thousands of United States dollars, except per share amounts)

Years ended December 31, 2018 and 2017

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.

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

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

	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
Revenue	\$ -	\$ -	\$ -	\$ -
Net loss	(6,814)	(10,262)	(5,531)	(6,261)
Basic and diluted loss per common share	(0.23)	(0.30)	(0.16)	(0.17)

	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
Revenue	\$ -	\$ -	\$ -	\$ -
Net loss	(3,292)	(2,441)	(2,640)	(3,270)
Basic and diluted loss per common share	(0.19)	(0.11)	(0.11)	(0.12)

**15. Comparative figures:**

Certain comparative figures in the years ended December 31, 2017 and December 31, 2016 have been reclassified in order to conform to US GAAP. On the statement of financial position, prepaid expenses and other current assets were previously presented on the statement of on a combined basis, as were account payables and accrued liabilities. Paid in capital was previously presented on the statement of financial position as Contributed Surplus and Stock options. On the statement of loss and comprehensive loss, foreign exchange gains and losses on marketable securities that were previously recorded in other income and expenses were reclassified to other comprehensive income. On the statement of cash flow, interest income, previously included in cash provided by or used in investing activities, is included in cash used from operating activities.

**16. Subsequent events**

(a) Subsequent to the year end, the Company issued 77,349 shares under the ATM for gross proceeds of US\$183 thousand. This transaction will be accounted for in the three months ended March 31, 2019.

(b) Subsequent to the year end, the Company issued 3,259,955 common shares under the Common Shares Purchase Agreement with Aspire Capital for gross proceeds of approximately \$6.0 million. This transaction will be accounted for in the three months ended March 31, 2019.

## Subsidiaries of the Registrant

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



KPMG LLP  
100 New Park Place, Suite 1400  
Vaughan, ON L4K 0J3  
Tel 905-265 5900  
Fax 905-265 6390  
www.kpmg.ca

**Consent of Independent Registered Public Accounting Firm**

The Board of Directors

Aptose Biosciences Inc.

We, KPMG LLP, consent to the incorporation by reference in the registration statement (No. 333-228794) on Form S-8 of Aptose Biosciences Inc. (the "Company") of our report dated March 12, 2019, with respect to the consolidated financial statements of Aptose Biosciences Inc. (the "Company"), which comprise the consolidated statements of financial position as at December 31, 2018 and December 31, 2017, the related consolidated statements of comprehensive loss and comprehensive loss, changes in shareholders' equity and cash flows for each of the years in the two-year period ended December 31, 2018, and the related notes (collectively, the "consolidated financial statements").

Our report dated March 12, 2019, contains an explanatory paragraph that states, without qualifying our opinion, that we draw attention to Note 2(a) and 15 to the consolidated financial statements, which indicates that the Company has retrospectively adopted United States generally accepted accounting principles (U.S. GAAP).

A handwritten signature in black ink that reads 'KPMG LLP' with a horizontal line underneath.

Chartered Professional Accountants, Licensed Public Accountants  
March 12, 2019  
Vaughan, Canada

KPMG LLP is a Canadian limited liability partnership and a member firm of the KPMG network of independent member firms affiliated with KPMG International Cooperative ("KPMG International"), a Swiss entity. KPMG Canada provides services to KPMG LLP.



**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 12, 2019

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

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

I, Gregory K. Chow, 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 12, 2019

/s/ Gregory K. Chow  
Name: Gregory K. Chow  
Title: Senior Vice President and Chief Financial  
Officer

**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, 2018 (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 12, 2019

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

**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, Gregory K. Chow, 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, 2018 (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 12, 2019

/s/ Gregory K. Chow  
Name: Gregory K. Chow  
Title: Senior Vice President and Chief Financial  
Officer