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

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended **September 30, 2022**

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

For the transition period from _____ to_____

Commission file number**: 001-37606**

ANAVEX LIFE SCIENCES CORP.

(Exact name of registrant as specified in its charter)

Nevada	98-0608404
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
630 5th Avenue, 20th Floor, New York, NY USA	10111
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code 1-844-689-3939

Securities registered under Section 12(b) of the Act:

Common Stock, $0.001 par value	AVXL	NASDAQ Stock Market LLC
Title of each class	Trading Symbol	Name of each exchange on which registered

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

Indicate by checkmark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.
Yes ☒ No ☐

Indicate by checkmark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act.
Yes ☐ No ☒

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

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

Indicate by checkmark 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 the definitions of "large accelerated filer," "accelerated filer", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☒
Accelerated filer ☐
Smaller reporting company ☐
Non-accelerated filer ☐
Emerging growth 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 the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal controls over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.
Yes ☒ No ☐

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

State the aggregate market value of the voting and non-voting 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 price of such common equity, as of the last business day of the registrant's most recently

completed second fiscal quarter: $921 million based on a price of $12.31 per share, being the closing price of the registrant's common stock on March 31, 2022.

Indicate the number of shares outstanding of each of the registrant's classes of common stock, as of the latest practicable date: 77,961,815 issued and outstanding as of November 28, 2022.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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Forward Looking Statements.

This Annual Report on Form 10-K includes forward-looking statements. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our anticipated future clinical and regulatory milestone events, future financial position, business strategy and plans and objectives of management for future operations, are forward-looking statements. The words "believe," "may," "estimate," "continue," "anticipate," "intend," "expect," "should," "forecast," "potential," "predict," "could," "would," "will," "suggest," "plan" and similar expressions, as they relate to us, are intended to identify forward-looking statements. Such forward-looking statements include, without limitation, statements regarding:

- volatility in our stock price and in the markets in general;
- our ability to successfully conduct preclinical studies and clinical trials for our product candidates;
- our ability to raise additional capital on favorable terms and the impact of such activities on our stockholders and stock price;
- the impact of the COVID-19 outbreak and its effect on us;
- our ability to generate any revenue or to continue as a going concern;
- our ability to execute our research and development plan on time and on budget;
- our products candidates' ability to demonstrate efficacy or an acceptable safety profile;
- our ability to obtain the support of qualified scientific collaborators;
- our ability, whether alone or with commercial partners, to successfully commercialize any of our product candidates that may be approved for sale;
- our ability to identify and obtain additional product candidates;
- our reliance on third parties in non-clinical studies and clinical trials;

- our ability to defend against product liability claims;
- our ability to safeguard against security breaches;
- our ability to obtain and maintain sufficient intellectual property protection for our product candidates;
- our ability to comply with our intellectual property licensing agreements;
- our ability to defend against claims of intellectual property infringement;
- our ability to comply with the maintenance requirements of the government patent agencies;
- our ability to protect our intellectual property rights throughout the world;
- competition;
- the anticipated start dates, durations and completion dates of our ongoing and future clinical trials;
- the anticipated designs of our future clinical trials;
- our ability to attract and retain qualified employees;
- the impact of Fast Track designation on receipt of actual FDA approval;
- our anticipated future regulatory submissions and our ability to receive regulatory approvals to develop and market our product candidates, including any orphan drug or Fast Track designations; and
- our anticipated future cash position and ability to obtain funding for our operations.

We have based these forward-looking statements largely on our current expectations and projections about future events, including the responses we expect from the U.S. Food and Drug Administration, ("FDA"), and other regulatory authorities and financial trends that we believe may affect our financial condition, results of operations, business strategy, preclinical and clinical trials, and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions including, without limitation, the risks described in "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K. These risks are not exhaustive. Other sections of this Annual Report on Form 10-K include additional factors which could adversely impact our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable laws including the securities laws of the United States, we assume no obligation to update or supplement forward-looking statements.

As used in this Annual Report on Form 10-K, the terms "we," "us," "our,", "Company" and "Anavex" mean Anavex Life Sciences Corp., unless the context clearly requires otherwise.

PART I

ITEM 1. BUSINESS

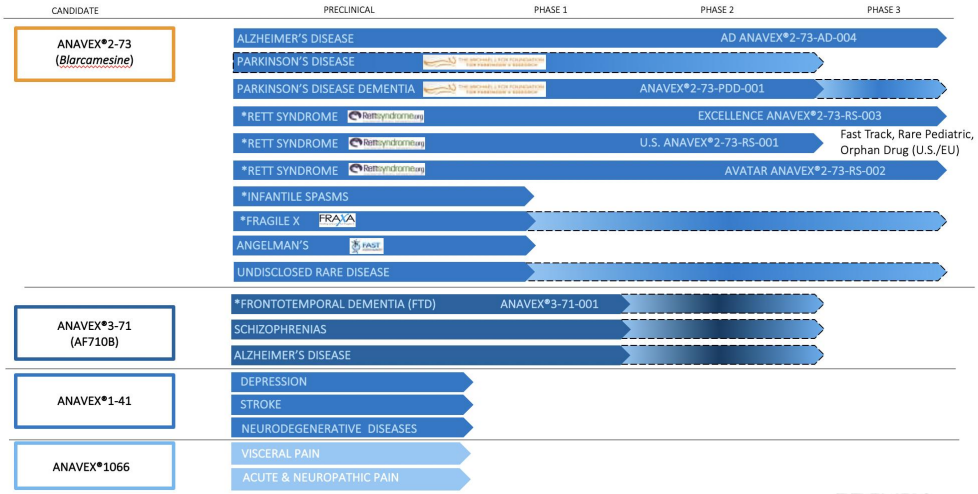
Overview and Strategy

Anavex Life Sciences Corp. is a clinical stage biopharmaceutical company engaged in the development of differentiated therapeutics by applying precision medicine to central nervous system ("CNS") diseases with high unmet need. We analyze genomic data from clinical trials to identify biomarkers, which we use in the analysis of our clinical trials.

Our lead product candidate, ANAVEX ®2-73, is being developed to treat Alzheimer's disease, Parkinson's disease and potentially other central nervous system diseases, including rare diseases, such as Rett syndrome, a rare severe neurological monogenic disorder caused by mutations in the X-linked gene, methyl-CpG-binding protein 2 ("MECP2").

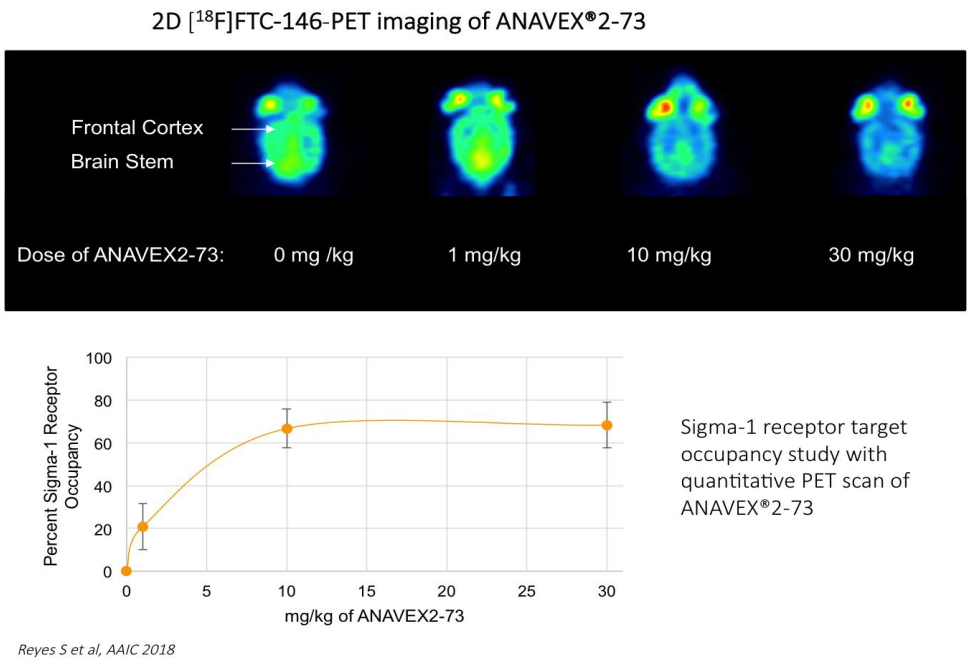
We currently have two core programs and two seed programs. Our core programs are at various stages of clinical and preclinical development, in neurodegenerative and neurodevelopmental diseases.

The following table summarizes key information about our programs:



** = Orphan Drug Designation by the FDA; Dashed lines indicate planned clinical trials to-date*

Anavex has a portfolio of compounds varying in sigma-1 receptor (SIGMAR1) binding activities. The SIGMAR1 gene encodes the SIGMAR1 protein, which is an intracellular chaperone protein with important roles in cellular communication. SIGMAR1 is also involved in transcriptional regulation at the nuclear envelope and restores homeostasis and stimulates recovery of cell function when activated. In order to validate the ability of our compounds to activate quantitatively the SIGMAR1, we performed, in collaboration with Stanford University, a quantitative Positron Emission Tomography (PET) imaging scan in mice, which demonstrated a dose-dependent ANAVEX®2-73 target engagement or receptor occupancy with SIGMAR1 in the brain.



Sigma-1 receptor target occupancy study with quantitative PET scan of ANAVEX®2-73

Source: Reyes S et al., Sci Rep. 2021 Aug 25;11(1):17150

Cellular Homeostasis

Many diseases are possibly directly caused by chronic homeostatic imbalances or cellular stress of brain cells. In pediatric diseases, such as Rett syndrome or infantile spasms, the chronic cellular stress is possibly caused by the presence of a constant genetic mutation. In neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases, chronic cellular stress is possibly caused by age-correlated buildup of cellular insult and hence chronic cellular stress. Specifically, defects in homeostasis of protein or ribonucleic acid ("RNA") lead to the death of neurons and dysfunction of the nervous system. The spreading of protein aggregates resulting in a proteinopathy, a characteristic found in Alzheimer's and Parkinson's diseases that results from disorders of protein synthesis, trafficking, folding, processing or degradation in cells. The clearance of macromolecules in the brain is particularly susceptible to imbalances that result in aggregation and degeneration in nerve cells. For example, Alzheimer's disease pathology is characterized by the presence of amyloid plaques, and neurofibrillary tangles, which are aggregates of hyperphosphorylated Tau protein that are a marker of other diseases known as tauopathies as well as inflammation of microglia. With the SIGMAR1 activation through SIGMAR1 agonists like ANAVEX®2-73, our approach is to restore cellular balance (i.e. homeostasis). Therapies that correct defects in cellular homeostasis might have the potential to halt or delay neurodevelopmental and neurodegenerative disease progression.

ANAVEX®2-73-specific Biomarkers

As part of some of our clinical trials, we have incorporated a genomic analysis to better understand potential populations for whom our clinical programs might benefit. In our clinical trials, a full genomic analysis of Alzheimer's disease patients treated with ANAVEX®2-73 has helped us identify actionable genetic variants. A significant impact of the genomic biomarkers SIGMAR1, the direct target of ANAVEX®2-73 and COMT, a gene involved in memory function, on the drug response level was identified, leading to an early ANAVEX®2-73-specific biomarker hypothesis. We believe that *excluding* patients with SIGMAR1 identified biomarker variant (approximately 10%-20% of the population) in prospective studies would identify approximately 80%-90% patients that would display clinically significant improved functional and cognitive scores. The consistency between the identified DNA and RNA data related to ANAVEX®2-73, which are considered independent of Alzheimer's disease pathology, as well as multiple endpoints and time-points, provides support for the potential precision medicine clinical development of ANAVEX®2-73 by using genetic biomarkers identified within the trial population itself to target patients who are most likely to respond to ANAVEX®2-73 treatment. We may in the future utilize such an approach in Alzheimer's disease as well as indications like Parkinson's disease dementia or Rett syndrome in which ANAVEX®2-73 is currently being studied.

Clinical Trials Overview

Alzheimer's Disease

In November 2016, we completed a Phase 2a clinical trial, consisting of Part A and Part B, which lasted a total of 57 weeks, for ANAVEX ®2-73 in mild-to-moderate Alzheimer's patients. This open-label, randomized trial in Australia met both primary and secondary endpoints and was designed to assess the safety and exploratory efficacy of ANAVEX®2-73 in 32 patients. ANAVEX®2-73 targets sigma-1 and muscarinic receptors, which have been shown in preclinical studies to reduce stress levels in the brain believed to restore cellular homeostasis and to reverse the pathological hallmarks observed in Alzheimer's disease. In October 2017, we presented positive pharmacokinetic ("PK") and pharmacodynamic ("PD") data from the Phase 2a clinical trial, which established a concentration-effect relationship between ANAVEX®2-73 and trial measurements. These measures obtained from all patients who participated in the entire 57 weeks include exploratory cognitive and functional scores as well as biomarker signals of brain activity. Additionally, the clinical trial appeared to show that ANAVEX®2-73 activity was enhanced by its active metabolite (ANAVEX19-144), which also targets the SIGMAR1 receptor and has a half-life approximately twice as long as the parent molecule.

Two consecutive trial extensions for the Phase 2a trial have allowed participants who completed the 52-week Part B of the trial to continue taking ANAVEX®2-73, providing us an opportunity to gather extended safety data for a cumulative time period of five years. In August 2020, patients completing these Phase 2a trial extensions were granted continued access to treatment with ANAVEX®2-73 through the Australian Government Department of Health – Therapeutic Goods Administration's compassionate use Special Access Scheme.

A larger Phase 2b/3 double-blind, placebo-controlled trial of ANAVEX ®2-73 in Alzheimer's disease commenced in August 2018. The Phase 2b/3 trial enrolled 509 patients for 48 weeks, randomized 1:1:1 to two different ANAVEX®2-73 doses or placebo. The trial commenced in Australia; and during fiscal 2020 additional regions were added in the United Kingdom, The Netherlands, Germany and Canada. Primary and secondary endpoints will assess safety and both cognitive and functional efficacy, measured through Alzheimer's Disease Assessment Scale – Cognition (ADAS-Cog), ADCS-ADL and Clinical Dementia Rating – Sum of Boxes for cognition and function (CDR-SB). In addition to the primary endpoints, the ANAVEX®2-73 Phase 2b/3 trial design incorporated pre-specified statistical analyses related to potential genomic precision medicine biomarkers identified in the ANAVEX®2-73 Phase 2a clinical trial. The trial completed enrollment in June 2021, exceeding the 450 patient enrollment target at 52 sites across Canada, Europe and Australia.

In October 2019, we initiated a long-term open label extension study of ANAVEX ®2-73, entitled the ATTENTION-AD trial, for patients who have completed the 48-week Phase 2b/3 placebo-controlled trial referenced above. This trial extension for an additional two years gives patients the opportunity to continue their treatment. Upon request by patients, caretakers and investigators, this extension trial was extended by one additional year.

Rett Syndrome

In February 2016, we presented positive preclinical data for ANAVEX ®2-73 in Rett syndrome, a rare neurodevelopmental disease. The data demonstrated dose related and significant improvements in an array of behavioral and gait paradigms in a mouse model with a MECP2-null mutation that causes neurological symptoms that mimic Rett syndrome. The study was funded by the International Rett Syndrome Foundation ("Rettsyndrome.org"). In January 2017, we were awarded a financial grant from Rettsyndrome.org of a minimum of $0.6 million to cover some of the costs of a multicenter Phase 2 clinical trial of ANAVEX®2-73 for the treatment of Rett syndrome. This award was received in quarterly instalments which commenced during fiscal 2018.

In March 2019, we commenced the first Phase 2 clinical trial in a planned Rett syndrome program of ANAVEX ®2-73 for the treatment of Rett syndrome. The clinical trials are being conducted in a range of patient age demographics and geographic regions, utilizing an oral liquid once-daily formulation of ANAVEX®2-73.

The first Phase 2 trial, (ANAVEX®2-73-RS-001), which took place in the United States, was completed in December 2020. This trial was a randomized double-blind, placebo-controlled safety, tolerability, PK and efficacy trial of oral liquid ANAVEX ®2-73 formulation in 25 adult female patients with Rett syndrome over a 7-week treatment period including ANAVEX®2-73-specific genomic precision medicine biomarkers. The primary endpoint of the trial was safety. The dosing of 5 mg ANAVEX®2-73 was well-tolerated and demonstrated dose-proportional PK. All secondary efficacy endpoints of the trial showed statistically significant and clinically meaningful response in the Rett Syndrome Behaviour Questionnaire ("RSBQ") response, when compared to placebo, in the intent to treat ("ITT") cohort (all participants, p = 0.011). 66.7% of ANAVEX®2-73 treated subjects showed a statistically significant improvement in RSBQ response as compared to 10% of the subjects on placebo in the ITT cohort (all participants, p = 0.011). ANAVEX®2-73 treatment resulted in a sustained improvement in Clinical Global Impression Improvement ("CGI-I") response throughout the 7-week clinical trial, when compared to placebo in the ITT cohort (all participants, p = 0.014). Consistent with previous ANAVEX®2-73 clinical trials, patients carrying the common form of the SIGMAR1 gene treated with ANAVEX®2-73 experienced stronger improvements in the prespecified efficacy endpoints.

The second, international trial of ANAVEX ®2-73 for the treatment of Rett syndrome, called the AVATAR trial, commenced in June 2019. This trial took place in Australia and the United Kingdom using a higher dose than the U.S. based Phase 2 trial for Rett syndrome. The trial was a Phase 3 randomized, double-blind, placebo-controlled trial to evaluate the safety and efficacy of ANAVEX®2-73 in 33 adult patients over a 7-week treatment period including ANAVEX®2-73 specific precision medicine biomarkers. Based upon the input from the successful U.S. Phase 2 Rett syndrome trial (ANAVEX®2-73-RS-001), we updated the endpoints for the AVATAR trial (ANAVEX®2-73-RS-002) to appropriately assess the clinically meaningful outcome following International Conference on Harmonization (ICH) guidelines. These updates were approved by the respective regulatory authorities in the U.K. and in Australia, respectively, where the AVATAR trial was conducted.

The data from the AVATAR trial was released in February 2022. The clinical trial met all primary and secondary efficacy and safety endpoints, with consistent improvements in primary efficacy endpoint, RSBQ response (p = 0.037), and secondary efficacy endpoints, ADAMS (p = 0.010) and CGI-I (p = 0.037) response. Efficacy endpoints demonstrated statistically significant and clinically meaningful reductions in Rett syndrome symptoms. Convenient once daily oral liquid doses of up to 30 mg of ANAVEX®2-73 were also well tolerated with good medication compliance. All patients who participated in the trial were eligible to receive ANAVEX®2-73 under a voluntary open label extension protocol.

In July 2020, we commenced the third trial of ANAVEX ®2-73 for the treatment of Rett syndrome, called the EXCELLENCE trial. This Phase 2/3 trial in pediatric patients with Rett syndrome includes trial sites in Australia, the United Kingdom, and Canada, and will evaluate the safety and efficacy of ANAVEX®2-73 in approximately 84 pediatric patients, aged 5 to 18, over a 12-week treatment period incorporating ANAVEX ®2-73 specific precision medicine biomarkers. All patients who participate in the trial will be eligible to receive ANAVEX®2-73 under a voluntary open label extension protocol, which is currently ongoing.

Parkinson's Disease

In September 2016, we presented positive preclinical data for ANAVEX ®2-73 in an animal model of Parkinson's disease, which demonstrated significant improvements on behavioral, histopathological, and neuroinflammatory endpoints. The study was funded by the Michael J. Fox Foundation. Additional data announced in October 2017 indicated that ANAVEX®2-73 induced robust neurorestoration in experimental Parkinsonism. We believe that the encouraging results we have gathered in this preclinical model, coupled with the favorable profile of this product candidate in the Alzheimer's disease trial, support the notion that ANAVEX®2-73 has the potential to treat Parkinson's disease dementia.

In October 2020, we completed a double-blind, randomized, placebo-controlled proof-of-concept Phase 2 trial with ANAVEX®2-73 in Parkinson's disease dementia in Spain and Australia, to study the effect of the compound on both the cognitive and motor impairment of Parkinson's disease. The Phase 2 trial enrolled approximately 132 patients for 14 weeks, randomized 1:1:1 to two different ANAVEX®2-73 doses, 30 mg and 50 mg, or placebo. The ANAVEX®2-73 Phase 2 Parkinson's disease dementia trial design incorporated genomic precision medicine biomarkers identified in the ANAVEX®2-73 Phase 2a Alzheimer's disease trial.

The trial demonstrated that ANAVEX®2-73 was safe and well tolerated in oral doses up to 50 mg once daily. The results showed clinically meaningful, dose-dependent, and statistically significant improvements in the Cognitive Drug Research ("CDR") computerized assessment system analysis. Treatment with ANAVEX®2-73 also resulted in clinically meaningful improvements as measured by the global composite score of Parkinson's disease symptom severity, MDS-Unified Parkinson's Disease Rating Scale total score on top of standard of care including dopaminergic therapy, levodopa and other anti-PD medications after 14 weeks of treatment, suggesting ANAVEX®2-73's potential capability of slowing and reversing symptoms that progress in Parkinson's disease. In addition, the trial confirmed the precision medicine approach of targeting SIGMAR1 as a genetic biomarker in response to ANAVEX®2-73 may result in improved clinical outcomes.

In January 2021, we were awarded a research grant of $1.0 million from The Michael J. Fox Foundation for Parkinson's Research to develop ANAVEX®2-73 for the treatment of Parkinson's disease. The award will explore utilization of PET imaging biomarkers to enable measurement of target engagement and pathway activation of the SIGMAR1 with clinically relevant doses in people with Parkinson's disease.

Frontotemporal Dementia

In July 2020, we commenced the First-in-Human Phase 1 clinical trial of ANAVEX®3-71. ANAVEX®3-71 was previously granted orphan drug designation for the treatment of Frontotemporal Dementia ("FTD") by the FDA. ANAVEX®3-71 is an orally administered small molecule targeting sigma-1 and M1 muscarinic receptors that is designed to be beneficial for neurodegenerative diseases. In preclinical studies, ANAVEX®3-71 demonstrated disease-modifying activity against the major hallmarks of Alzheimer's disease in transgenic (3xTg-AD) mice, including cognitive deficits, amyloid and tau pathologies, as well as beneficial effects on mitochondrial dysfunction and neuroinflammation.

The Phase 1 clinical trial was a prospective double-blind, randomized, placebo-controlled trial in Australia. A total of 36 healthy male and female subjects were included. Single escalating doses of ANAVEX®3-71 were administered in order to evaluate the safety, tolerability, and PK of ANAVEX®3-71 and the effects of food and gender on its PK in healthy volunteers.

The trial met its primary and secondary endpoints of safety, with no serious adverse events ("SAEs") or dose-limiting toxicities observed. ANAVEX®3-71 was well tolerated in all cohorts receiving ANAVEX®3-71 in single doses ranging from 5 mg to 200 mg daily with no SAEs and no significant lab abnormalities in any subject. In the trial, ANAVEX®3-71 exhibited linear PK. Its pharmacokinetics was also dose proportional for doses up to 160 mg. Gender had no effect on the PK of the drug and food had no effect on the bioavailability of ANAVEX®3-71. The trial also met the secondary objective of characterizing the effect of ANAVEX®3-71 on electrocardiogram ("ECG") parameters. There were no clinically significant ECG parameters throughout the trial. Participant QTcF measures were normal across all dose groups with no difference between ANAVEX®3-71 and placebo.

Based on these results, and ANAVEX®3-71's pre-clinical profile, we intend to advance ANAVEX®3-71 into a biomarker-driven clinical development dementia program for the treatment of schizophrenia, FTD and Alzheimer's disease, evaluating longitudinal effect of treatment with ANAVEX®3-71. We believe the results of these clinical trials and preclinical study could serve as the basis for advancing into respective registration studies in the U.S.

Our Pipeline

Our research and development pipeline includes ANAVEX ®2-73 currently in three different clinical trial indications, and several other compounds in different stages of clinical and pre-clinical development.

Our proprietary SIGMACEPTOR™ Discovery Platform produced small molecule drug candidates with unique modes of action, based on our understanding of sigma receptors. Sigma receptors may be targets for therapeutics to combat many human diseases, both of neurodegenerative nature, including Alzheimer's disease, as well as of neurodevelopmental nature, like Rett syndrome. When bound by the appropriate ligands, sigma receptors influence the functioning of multiple biochemical signals that are involved in the pathogenesis (origin or development) of disease. Multiple viruses including SARS-CoV-2 (COVID-19) induce cellular stress by intrinsic mitochondrial apoptosis and other related cellular processes, in order to ensure survival and replication. Hence, it is possible that SIGMAR1 could play a role in modulating the cellular response to viral infection and ameliorate pathogenesis.

Compounds that have been subjects of our research include the following:

ANAVEX®2-73 *(blarcamesine)*

We believe ANAVEX®2-73 may offer a disease-modifying approach in neurodegenerative and neurodevelopmental diseases by activation of SIGMAR1. ANAVEX®2-73 is being developed in an oral liquid once-daily formulation for rare diseases such as Rett syndrome as well as an oral once-daily capsule formulation for diseases such as Alzheimer's disease.

In Rett syndrome, administration of ANAVEX ®2-73 in liquid form resulted in both significant and dose related improvements in an array of behavioral paradigms in the MECP2 HET Rett syndrome disease model. In addition, in a further experiment sponsored by Rettsyndrome.org, ANAVEX®2-73 was evaluated in automatic visual response and respiration tests in 7-month old mice, an age at which advanced pathology is evident. Vehicle-treated MECP2 mice demonstrated fewer automatic visual responses than wild-type mice. Treatment with ANAVEX®2-73 for four weeks significantly increased the automatic visual response in the MECP2 Rett syndrome disease mice. Additionally, chronic oral dosing daily for 6.5 weeks of ANAVEX®2-73 starting at ~5.5 weeks of age was conducted in the MECP2 HET Rett syndrome disease mouse model assessed the different aspects of muscular coordination, balance, motor learning and muscular strengths, some of the core deficits observed in Rett syndrome. Administration of ANAVEX®2-73 resulted in both significant and dose related improvements in an array of these behavioral paradigms in the MECP2 HET Rett syndrome disease model.

In May 2016 and June 2016, the FDA granted Orphan Drug Designation to ANAVEX ®2-73 for the treatment of Rett syndrome and infantile spasms, respectively. In November 2019, the FDA granted to ANAVEX®2-73 the Rare Pediatric Disease (RPD) designation for the treatment of Rett syndrome. The RPD designation is intended to encourage the development of treatments for rare pediatric diseases.

Further, in February 2020, the FDA granted Fast Track designation for the ANAVEX ®2-73 clinical development program for the treatment of Rett syndrome. The FDA Fast Track program is designed to facilitate and expedite the development and review of new drugs to address unmet medical needs in the treatment of serious and life-threatening conditions.

For Parkinson's disease, data demonstrates significant improvements and restoration of function in a disease modifying animal model of Parkinson's disease. Significant improvements were seen on all measures tested: behavioral, histopathological, and neuroinflammatory endpoints. In October 2020, we completed a double-blind, randomized, placebo-controlled proof-of-concept Phase 2 trial with ANAVEX®2-73 in Parkinson's disease dementia, to study the effect of the compound on both the cognitive and motor impairment of Parkinson's disease. The Phase 2 trial enrolled approximately 132 patients for 14 weeks, randomized 1:1:1 to two different ANAVEX®2-73 doses, 30 mg and 50 mg, or placebo. The ANAVEX ®2-73 Phase 2 Parkinson's disease dementia trial design incorporated genomic precision medicine biomarkers identified in the ANAVEX®2-73 Phase 2a Alzheimer's disease trial.

The trial demonstrated that ANAVEX®2-73 was safe and well tolerated in oral doses up to 50 mg once daily. The results showed clinically meaningful, dose-dependent, and statistically significant improvements in the CDR computerized assessment system analysis. We anticipate conducting further clinical trials of ANAVEX®2-73 in Parkinson's disease dementia after submitting the results of the trial to the FDA to obtain regulatory guidance.

In Alzheimer's disease animal models, ANAVEX®2-73 has shown pharmacological, histological and behavioral evidence as a potential neuroprotective, anti-amnesic, anti-convulsive and anti-depressive therapeutic agent, due to its potent affinity to SIGMAR1 and moderate affinities to M1-4 type muscarinic receptors. In addition, ANAVEX®2-73 has shown a potential dual mechanism which may impact amyloid, tau pathology and inflammation. In a transgenic Alzheimer's disease animal model Tg2576, ANAVEX®2-73 induced a statistically significant neuroprotective effect against the development of oxidative stress in the mouse brain, as well as significantly increased the expression of functional and synaptic plasticity markers that is apparently amyloid-beta independent. It also statistically alleviated the learning and memory deficits developed over time in the animals, regardless of sex, both in terms of spatial working memory and long-term spatial reference memory.

Based on the results of pre-clinical testing, we initiated and completed a Phase 1 single ascending dose (SAD) clinical trial of ANAVEX ®2-73. In this Phase 1 SAD trial, the maximum tolerated single dose was defined per protocol as 55-60 mg. This dose is above the equivalent dose shown to have positive effects in mouse models of Alzheimer's disease. There were no significant changes in laboratory or ECG parameters. ANAVEX®2-73 was well tolerated below the 55-60 mg dose with only mild adverse events in some subjects. Observed adverse events at doses above the maximum tolerated single dose included headache and dizziness, which were moderate in severity and reversible. These side effects are often seen with drugs that target CNS conditions, including Alzheimer's disease.

In November 2016, we completed a Phase 2a clinical trial for ANAVEX ®2-73, for the treatment of Alzheimer's disease. The open-label randomized trial was designed to assess the safety and exploratory efficacy of ANAVEX®2-73 in 32 patients with mild-to-moderate Alzheimer's disease. The Phase 2a trial met both primary and secondary objectives of the trial.

In July 2018, we presented the results of a genomic DNA and RNA evaluation of the participants in the Phase 2a clinical trial. More than 33,000 genes were analyzed using unbiased, data driven, machine learning, artificial intelligence (AI) system for analyzing DNA and RNA data in patients treated with ANAVEX®2-73. The analysis identified genetic variants that impacted response to ANAVEX ®2-73, among them variants related to the SIGMAR1, the target for ANAVEX®2-73. Results showed that trial participants with the common SIGMAR1 wild type gene variant, which is estimated to be about 80% of the population worldwide, demonstrated improved cognitive (MMSE) and the functional (ADCS-ADL) scores. The results from this evaluation supported the continued evaluation of genomic information in subsequent clinical trials, since these signatures can now be applied to neurological indications tested in future clinical trials with ANAVEX®2-73 including Alzheimer's disease, Parkinson's disease dementia and Rett syndrome.

ANAVEX®2-73 data met prerequisite information in order to progress into a Phase 2b/3 placebo-controlled trial. On July 2, 2018, the Human Research Ethics Committee in Australia approved the initiation of our Phase 2b/3, double-blind, randomized, placebo-controlled 48-week safety and efficacy trial of ANAVEX®2-73 for the treatment of early Alzheimer's disease. Clinical trial sites in Canada, the United Kingdom, the Netherlands and Germany were also added. This Phase 2b/3 trial design incorporates inclusion of genomic precision medicine biomarkers identified in the ANAVEX®2-73 Phase 2a trial. The Phase 2b/3 trial, which has completed enrollment, randomized 1:1:1 to either two different ANAVEX®2-73 doses or placebo.

We believe preclinical data from our studies also supports ANAVEX ®2-73 as a potential platform drug for other neurodegenerative diseases beyond Alzheimer's disease, Parkinson's disease or Rett syndrome, more specifically, epilepsy, infantile spasms, Fragile X syndrome, Angelman syndrome, multiple sclerosis and, more recently, tuberous sclerosis complex (TSC). ANAVEX®2-73 demonstrated significant improvements in all of these indications in the respective preclinical animal models.

In a preclinical study sponsored by the Foundation for Angelman Syndrome, ANAVEX ®2-73 was assessed in a mouse model for the development of audiogenic seizures. The results indicated that ANAVEX®2-73 administration significantly reduced audiogenic-induced seizures. In a study sponsored by FRAXA Research Foundation regarding Fragile X syndrome, data demonstrated that ANAVEX®2-73 restored hippocampal brain-derived neurotrophic factor (BDNF) expression to normal levels. BDNF under-expression has been observed in many neurodevelopmental and neurodegenerative pathologies. BDNF signaling promotes maturation of both excitatory and inhibitory synapses. ANAVEX®2-73 normalization of BDNF expression could be a contributing factor for the positive data observed in both neurodevelopmental and neurodegenerative disorders like Angelman and Fragile X syndromes.

In addition, preclinical data to-date also indicates that ANAVEX ®2-73 has the potential to demonstrate protective effects of mitochondrial enzyme complexes during pathological conditions, which, if impaired, are believed to play a role in the pathogenesis of neurodegenerative and neurodevelopmental diseases.

In addition, preclinical data on ANAVEX ®2-73 related to multiple sclerosis indicates that ANAVEX ®2-73 may promote remyelination in multiple sclerosis disease. Further, our data also demonstrates that ANAVEX®2-73 has the potential to provide protection for oligodendrocytes ("OL's") and oligodendrocyte precursor cells ("OPC's"), as well as central nervous system neurons in addition to helping repair by increasing OPC proliferation and maturation in tissue culture.

In March 2018, we presented preclinical data of ANAVEX ®2-73 in a genetic mouse model of tuberous sclerosis complex ("TSC"). TSC is a rare genetic disorder characterized by the growth of numerous benign tumors in many parts of the body with a high incidence of seizures. The preclinical data demonstrated that treatment with ANAVEX®2-73 significantly increased survival and reduced seizures in those mice.

ANAVEX®3-71

ANAVEX®3-71 is a clinical drug candidate with a novel mechanism of action via SIGMAR1 activation and M1 muscarinic allosteric modulation, which has been shown to enhance neuroprotection and cognition in Alzheimer's disease models. ANAVEX®3-71 is a CNS-penetrable potential disease modifying treatment for cognitive impairments. We believe it is effective in very small doses against the major Alzheimer's hallmarks in transgenic (3xTg-AD) mice, including cognitive deficits, amyloid and tau pathologies, and also has beneficial effects on inflammation and mitochondrial dysfunctions. ANAVEX®3-71 indicates extensive therapeutic advantages in Alzheimer's and other protein-aggregation-related diseases given its ability to enhance neuroprotection and cognition via SIGMAR1 activation and M1 muscarinic allosteric modulation.

A preclinical study examined the response of ANAVEX ®3-71 in aged transgenic animal models and showed a significant reduction in the rate of cognitive deficit, amyloid beta pathology and inflammation with the administration of ANAVEX 3-71. In April 2016, the FDA granted Orphan Drug Designation to ANAVEX®3-71 for the treatment of FTD.

During pathological conditions ANAVEX®3-71 demonstrated the formation of new synapses between neurons (synaptogenesis) without causing an abnormal increase in the number of astrocytes. In neurodegenerative diseases such as Alzheimer's and Parkinson's disease, synaptogenesis is believed to be impaired. Additional preclinical data presented also indicates that in addition to reducing oxidative stress, ANAVEX®3-71 has the potential to demonstrate protective effects of mitochondrial enzyme complexes during pathological conditions, which, if impaired, are believed to play a role in the pathogenesis of neurodegenerative and neurodevelopmental diseases.

In July 2020, we commenced the first Phase 1 clinical trial of ANAVEX ®3-71. The trial took place in Australia and was a double-blind, randomized, placebo-controlled, Phase 1 trial to evaluate safety and tolerability, and PK of oral escalating doses of ANAVEX®3-71 including effects of food and gender in healthy volunteers. The trial met its primary and secondary endpoints of safety, respectively with no serious adverse events (SAEs) or dose-limiting toxicities observed, as more fully described above under *Clinical Trials Overview – Frontotemporal Dementia*.

Based on these results, and ANAVEX ®3-71 pre-clinical profile, the Company intends to advance ANAVEX ®3-71 into a biomarker-driven clinical development dementia program for the treatment of schizophrenia, FTD and Alzheimer's disease, evaluating longitudinal effect of treatment with ANAVEX®3-71. We believe the results of this clinical trial and preclinical study could serve as a basis for advancing into respective registration trials in the U.S.

ANAVEX®1-41

ANAVEX®1-41 is a sigma-1 agonist. Pre-clinical tests revealed significant neuroprotective benefits (i.e., protects nerve cells from degeneration or death) through the modulation of endoplasmic reticulum, mitochondrial and oxidative stress, which damages and impairs cell viability. In addition, in animal models, ANAVEX®1-41 prevented the expression of caspase-3, an enzyme that plays a key role in apoptosis (programmed cell death) and loss of cells in the hippocampus, the part of the brain that regulates learning, emotion and memory. These activities involve both muscarinic and SIGMAR1 systems through a novel mechanism of action.

Preclinical data presented also indicates that ANAVEX ®1-41 has the potential to demonstrate protective effects of mitochondrial enzyme complexes during pathological conditions, which, if impaired, are believed to play a role in the pathogenesis of neurodegenerative and neurodevelopmental diseases.

ANAVEX®1066

ANAVEX®1066, a mixed sigma-1/sigma-2 ligand is designed for the potential treatment of neuropathic and visceral pain. ANAVEX ®1066 was tested in two preclinical models of neuropathic and visceral pain that have been extensively validated in rats. In the chronic constriction injury model of neuropathic pain, a single oral administration of ANAVEX®1066 dose-dependently restored the nociceptive threshold in the affected paw to normal levels while leaving the contralateral healthy paw unchanged. Efficacy was rapid and remained significant for two hours. In a model of visceral pain, chronic colonic hypersensitivity was induced by injection of an inflammatory agent directly into the colon and a single oral administration of ANAVEX®1066 returned the nociceptive threshold to control levels in a dose-dependent manner. Companion studies in rats demonstrated the lack of any effects on normal gastrointestinal transit with ANAVEX®1066 and a favorable safety profile in a battery of behavioral measures.

ANAVEX®1037

ANAVEX®1037 is designed for the treatment of prostate and pancreatic cancer. It is a low molecular weight, synthetic compound exhibiting high affinity for SIGMAR1 at nanomolar levels and moderate affinity for sigma-2 receptors and sodium channels at micromolar levels. In advanced pre-clinical studies, this compound revealed antitumor potential. It has also been shown to selectively kill human cancer cells without affecting normal/healthy cells and also to significantly suppress tumor growth in immune-deficient mice models. Scientific publications highlight the possibility that these ligands may stop tumor growth and induce selective cell death in various tumor cell lines. Sigma receptors are highly expressed in different tumor cell types. Binding by appropriate sigma-1 and/or sigma-2 ligands can induce selective apoptosis. In addition, through tumor cell membrane reorganization and interactions with ion channels, we believe our drug candidates may play an important role in inhibiting the processes of metastasis (spreading of cancer cells from the original site to other parts of the body), angiogenesis (the formation of new blood vessels) and tumor cell proliferation.

ANAVEX®1037 is currently in the pre-clinical and clinical testing stages of development, and there is no guarantee that the activity demonstrated in pre-clinical models will be shown in human testing.

We continue to identify and initiate discussions with potential strategic and commercial partners to most effectively advance our programs and increase stockholder value. Further, we may acquire or develop new intellectual property and assign, license, or otherwise transfer our intellectual property to further our goals.

Our Target Indications

We are developing compounds with potential application to two broad categories and several specific indications, including:

Central Nervous System Diseases

- Alzheimer's disease – In 2022, an estimated 6.5 million Americans were suffering from Alzheimer's disease. The Alzheimer's Association ® estimates that by 2050, this number is expected to rise to 12.7 million Americans. Medications on the market today treat only the symptoms of Alzheimer's disease and do not have the ability to stop its onset or its progression. We believe there is an urgent and unmet need for both a disease modifying cure for Alzheimer's disease as well as for better symptomatic treatments.

- Parkinson's disease – Parkinson's disease is a progressive disease of the nervous system marked by tremors, muscular rigidity, and slow, imprecise movement. It is associated with degeneration of the basal ganglia of the brain and a deficiency of the neurotransmitter dopamine. Parkinson's disease currently is estimated to afflict more than 10 million people worldwide, typically middle-aged and elderly people. The Parkinson's disease market is expected to reach to $11.5 billion by 2029, according to GlobalData.

- Rett syndrome – Rett syndrome is a rare X-linked genetic neurological and developmental disorder that affects the way the brain develops, including protein transcription, which is altered and as a result leads to severe disruptions in neuronal homeostasis. It is considered a rare, progressive neurodevelopmental disorder and is caused by a single mutation in the MECP2 gene. Because males have a different chromosome combination from females, boys who have the genetic MECP2 mutation are affected in devastating ways. Most of them die before birth or in early infancy. For females who survive infancy, Rett syndrome leads to severe impairments, affecting nearly every aspect of the child's life; severe mental retardation, their ability to speak, walk and eat, sleeping problems, seizures and even the ability to breathe easily. Rett syndrome affects approximately 1 in every 10,000-15,000 females.

- Depression – Depression is a major cause of morbidity worldwide according to the World Health Organization. The global antidepressant drug market is projected to reach $21 Billion by 2030 according to Allied Market Research. Pharmaceutical treatment for depression has been historically dominated by blockbuster brands. However, the dominance of the leading brands is waning, largely due to an increase in the number of approvals for antidepressant drugs.

- Epilepsy – Epilepsy is a common chronic neurological disorder characterized by recurrent unprovoked seizures. These seizures are transient signs and/or symptoms of abnormal, excessive or synchronous neuronal activity in the brain. According to the Centers for Disease Control and Prevention, in 2015 epilepsy affected 3.4 million Americans. Today, epilepsy is often controlled, but not cured, with medication that is categorized as older traditional anti-epileptic drugs and second generation anti-epileptic drugs. Because epilepsy afflicts sufferers in different ways, there is a need for drugs used in combination with both traditional anti-epileptic drugs and second generation anti-epileptic drugs.

- Neuropathic Pain – We define neuralgia, or neuropathic pain, as pain that is not related to activation of pain receptor cells in any part of the body. Neuralgia is more difficult to treat than some other types of pain because it does not respond well to normal pain medications. Special medications have become more specific to neuralgia and typically fall under the category of membrane stabilizing drugs or antidepressants.

Cancer

- Malignant Melanoma – Predominantly a skin cancer, malignant melanoma can also occur in melanocytes found in the bowel and the eye. Malignant melanoma accounts for a large majority of skin cancer deaths. The treatment includes surgical removal of the tumor, adjuvant treatment, chemo and immunotherapy, or radiation therapy. According to iHealthcareAnalyst, Inc. the worldwide malignant melanoma market is expected to grow to $7.5 billion by 2029.

- Prostate Cancer – Specific to men, prostate cancer is a form of cancer that develops in the prostate, a gland in the male reproductive system. Cancer cells may metastasize from the prostate to other parts of the body, particularly the bones and lymph nodes. Drug therapeutics for prostate cancer are expected to increase to nearly $10.1 billion by the end of 2030 according to Market Research Future.

- Pancreatic Cancer – Pancreatic cancer is a malignant neoplasm of the pancreas. In the United States, approximately 62,000 new cases of pancreatic cancer will be diagnosed this year and approximately 50,000 patients will die as a result of their cancer, according to the American Cancer Society. Sales predictions by Market Data Forecast predict that the market for the global pharmaceutical treatment of pancreatic cancer will increase from $2.59 billion in 2022 to $3.73 billion by 2027.

Competition

The drug discovery and development industry is very competitive, characterized by rapid advancements in technology, where protection of proprietary advancements is essential. Any product candidates that we may successfully develop and commercialize, may compete with existing therapies, or new therapies that may become available in the future. Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer side effects, are more convenient or are less expensive than any products that we may develop.

We believe our approach to the treatment of Alzheimer's disease and other CNS diseases differs from our competitors - our platform may offer a disease-modifying approach in neurodegenerative and neurodevelopmental diseases by activation of SIGMAR1. In our preclinical studies, when activated by SIGMAR1 agonists, such as ANAVEX®2-73, SIGMAR1 demonstrated reduced cellular stress before and after RNA gene transcription. Our studies confirm the potential existence of a predictive biomarker of response established through SIGMAR1 mRNA expression that could be used in future clinical trials. Because of its role in maintaining neuronal homeostasis, we believe sigma receptors show significant promise as viable targets for therapeutic molecules in an effort to treat Alzheimer's disease and other CNS diseases and disorders, including Parkinson's disease and Rett syndrome, by restoring healthy gene expression.

At this time, our competitors are primarily other biomedical development companies that are aiming to discover and develop compounds to be used in the treatment of Alzheimer's disease and other CNS diseases, and those companies already doing so. We also face competition from academic institutions and government agencies, both in the United States and abroad.

Our competitors may have significantly greater financial resources, an established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, may be in the process of obtaining regulatory approvals and marketing of approved products. These competitors also compete with us in recruiting and retaining qualified scientific and technical personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring or developing technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

For additional discussion of the risks related to competition, see Item 1A "Risk Factors."

Patents, Trademarks and Intellectual Property

We hold ownership or exclusive rights to seventeen U.S. patents, nineteen U.S. patent applications, and various PCT or ex-U.S. patent applications relating to our drug candidates, methods associated therewith, and to our research programs.

We own one issued U.S. patent entitled "ANAVEX ®2-73 and certain anticholinesterase inhibitors composition and method for neuroprotection" claims a composition of matter of ANAVEX®2-73 directed to a novel and synergistic neuroprotective compound combined with donepezil and other cholinesterase inhibitors. This patent is expected to expire in June 2034, absent any patent term extension for regulatory delays. We own three issued U.S. patents each with claims directed to crystalline forms of ANAVEX®2-73. The first of these three patents claims crystalline forms of ANAVEX ®2-73, dosage forms and compositions containing crystalline ANAVEX®2-73, and methods of treatment for Alzheimer's disease using them. This patent is expected to expire in July 2036, absent any patent term extension for regulatory delays. The second of these three patents claims pharmaceutical compositions containing a crystalline form of ANAVEX®2-73, and methods of treatment for Alzheimer's disease using the compositions. This patent is expected to expire in June 2037, absent any patent term extension for regulatory delays. The third of these three patents claims pharmaceutical compositions containing a crystalline form of ANAVEX®2-73, and methods of treatment for Alzheimer's disease using the compositions. This patent is expected to expire in June 2037, absent any patent term extension for regulatory delays. We also own two issued U.S. patents for seizure treatment. The first of these two patents claims methods and dosage forms for treating seizures, the dosage forms containing a low-dose anti-epilepsy drug combined with either: (i) ANAVEX®2-73 and its active metabolite ANAVEX®19-144; or (ii) ANAVEX ®19-144. The second of these two patents further claims a combination seizure treatment involving administration of an anti-epilepsy drug combined with (i) ANAVEX®19-144, or (ii) ANAVEX 19-144 ® and ANAVEX 2-73 ®. Both patents are expected to expire in October 2035, absent any patent term extension for regulatory delays. We also own three issued U.S. patents with claims directed to treating neurodevelopmental disorders. These patents claim methods for treating a neurodevelopmental disorder, multiple sclerosis, or their related biochemical and functional abnormalitiesby administering ANAVEX®2-73, ANAVEX®19-144, and/or ANAVEX®1-41 (another sigma receptor ligand similar to ANAVEX®2-73), or compositions thereof. All three patents are expected to expire in January 2037, absent any patent term extension for regulatory delays. In addition, we own one issued U.S. Patent with claims directed to methods of treating melanoma with a compound related to ANAVEX®2-73. This patent is expected to expire in February 2030, absent any patent term extension for regulatory delays. We also own an issued U.S. patent that claims crystalline forms of ANAVEX®19-144, dosage forms and compositions containing the crystalline forms of ANAVEX ®19-144, and methods of treatment for Alzheimer's disease. This patent is expected to expire in July 2036, absent any patent term extension for regulatory delays. Further, we own one issued U.S. Patent with claims directed to methods of treating cardiac dysfunction with ANAVEX®2-73. This patent is expected to expire in July 2038, absent any patent term extension for regulatory delays. Additionally, we own one issued U.S. Patent with claims directed to methods of treating insomnia or anxiety with ANAVEX®2-73, ANAVEX®19-144, and/or ANAVEX®1-41. This patent is expected to expire in September 2038, absent any patent term extension for regulatory delays.

We also own two issued U.S. patents related to ANAVEX ®1066. The first of these two patents claims methods for treating or preventing pain using (+) ANAVEX®1066 isomer. The second patent claims methods for treating or preventing pain using (-) ANAVEX ®1066 isomer. Both patents are expected to expire in November 2036, absent any patent term extension for regulatory delays.

For ANAVEX®2-73, ANAVEX®19-144, ANAVEX®1-41, and ANAVEX ®1066, we also have granted or pending applications in Australia, Canada, China, Europe, Japan, and Hong Kong, which are expected to expire after 2035.

With regard to ANAVEX ®3-71, we own exclusive rights to two issued U.S. patents with claims respectively directed to the ANAVEX ®3-71 compound and methods of treating various diseases including Alzheimer's with the same. These patents are expected to expire in April 2030, and January 2030, respectively, absent any patent term extension for regulatory delays. We also own exclusive rights to related patents or applications that are granted or pending in Australia, Canada, China, Europe, Japan, Korea, New Zealand, Russia, and South Africa, which are expected to expire in January 2030.

We also own other patent applications directed to enantiomers, crystals, formulations, uses, and patient selection methods that may provide additional protection for one or more of our product candidates.

We regard patents and other intellectual property rights as corporate assets. Accordingly, we attempt to optimize the value of intellectual property in developing our business strategy including the selective development, protection, and exploitation of our intellectual property rights. In addition to filings made with intellectual property authorities, we protect our intellectual property and confidential information by means of carefully considered processes of communication and the sharing of information, and by the use of confidentiality and non-disclosure agreements and provisions for the same in contractor's agreements. While no agreement offers absolute protection, such agreements provide some form of recourse in the event of disclosure, or anticipated disclosure.

Our intellectual property position, like that of many biomedical companies, is uncertain and involves complex legal and technical questions for which important legal principles are unresolved. For more information regarding challenges to our existing or future patents, see "Risk Factors".

Government regulation

Government authorities in the United States, at the federal, state and local levels, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the NDA or ANDA process before it may be legally marketed in the United States. We are subject to various government regulations in connection with the development of our pipeline.

U.S. Drug Development and Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act and its implementing regulations ("FDCA"). The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, import refusal, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Once a drug candidate is identified for development, it enters the preclinical testing stage and an Investigational New Drug Application ("IND") may be opened for the regulatory development of the product. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as other preclinical studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND to conduct clinical trials. The sponsor must also include a protocol detailing, among other things, the objectives of the first phase of clinical trials, the parameters to be used in monitoring the safety of the trial, and the effectiveness criteria to be evaluated should the first phase lend itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is filed. The IND automatically becomes effective thirty (30) days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about ongoing or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with FDA good clinical practice ("GCP") requirements, which include a requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection inclusion and exclusion criteria and the safety and/or effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. An Institutional Review Board ("IRB") at each institution participating in the clinical trial must review and approve each protocol before a clinical trial may commence at the institution and must also approve the information regarding the trial as well as the informed consent form that must be provided to each trial participant or his or her legal representative, monitor the study until completed and otherwise comply with all applicable IRB regulations.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined in certain cases:

Phase 1: The compound is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness. In most cases, initial Phase 1 clinical trials are conducted with healthy volunteers. However, where the compound being evaluated is for the treatment of severe or life-threatening diseases, such as cancer, and especially when the product may be too toxic to ethically administer to healthy volunteers, the initial human testing may be conducted on patients with the target disease or condition. Sponsors sometimes subdivide their Phase 1 clinical trials into Phase 1a and Phase 1b clinical trials. Phase 1b clinical trials are typically aimed at confirming dosage, PK and safety in a larger number of patients. Some Phase 1b clinical trials evaluate biomarkers or surrogate markers that may be associated with efficacy in patients with specific types of diseases or conditions.

Phase 2: This phase involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases or conditions and to confirm dosage tolerance and appropriate dosage.

Phase 3: Phase 3 clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population, generally at geographically dispersed clinical trial sites. These clinical trials, often referred to as "pivotal" or "confirmatory" clinical trials, are intended to establish the overall risk-benefit ratio of the compound and provide, if appropriate, an adequate basis for product approval and labeling.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including any finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected, serious harm to study subjects. In addition, clinical trials may be overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this board or committee may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

Phase 4: Phase 4 or post-approval trials may also be conducted after a drug receives initial marketing approval. These trials, often referred to as "Phase 4" trials, are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of such clinical trials as a condition of approval of continued marketing of the product.

During the development of a new drug, sponsors are given several opportunities to meet with the FDA. These meetings can provide an opportunity for the sponsor to share information about the progress of the application or clinical trials, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. These meetings may occur prior to the submission of an IND, at the end of Phase 2 clinical trials, or before an NDA is ultimately submitted. Sponsors typically use the meetings at the end of the Phase 2 trials to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug. Meetings at other times may be made upon request and are subject to approval by the FDA.

Concurrent with clinical trials, companies typically complete additional, animal or other non-clinical studies, develop additional information about the chemistry and physicochemical characteristics of the drug, and finalize a process for manufacturing the product in commercial quantities in accordance with the FDA's current Good Manufacturing Practices ("cGMP") requirements. The manufacturing process must consistently produce quality batches of the drug and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate the effectiveness of the packaging and that the compound does not undergo unacceptable deterioration over its shelf life.

While the IND is active, progress reports summarizing the results of ongoing clinical trials and nonclinical studies performed since the last progress report must be submitted on at least an annual basis to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important, increased incidence of a serious adverse reaction compared to that listed in the protocol or investigator brochure.

There are also requirements governing the submission of certain clinical trials and completed trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose specified clinical trial registration and results information, which is made publicly available at www.clinicaltrials.gov. Failure to properly report clinical trial results can result in civil monetary penalties. Disclosure of clinical trial results can often be delayed until the new product or new indication being studied has been approved.

U.S. review and approval process

The results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of a New Drug Application ("NDA"). The submission of an NDA is subject to the payment of substantial user fees; a waiver of which may be obtained under certain limited circumstances.

The FDA reviews NDAs to determine, among other things, whether the product is safe and effective for its intended use and whether it is manufactured in a cGMP-compliant manner, which will assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act ("PDUFA"), the FDA has a goal of ten months from the date of "filing" of a standard, completed NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted. The FDA conducts a preliminary review of all NDAs within the first sixty days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

The FDA may refer an application for a new drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether and under what conditions the application should be approved. The FDA is not bound by the recommendations of such an advisory committee, but it considers advisory committee recommendations carefully when making decisions.

Before approving an NDA, the FDA will also inspect the facility where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. Before approving an NDA, the FDA may also inspect one or more clinical trial sites to assure compliance with GCP requirements and inspect the clinical trial records.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase 3 trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies or product manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications.

The Pediatric Research Equity Act ("PREA"), requires IND sponsors to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or the FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

If a drug receives FDA approval, the approval may be limited to specific diseases and dosages, which could restrict the commercial value of the product. In addition, the FDA may require testing and surveillance programs to monitor the safety of approved products which have been commercialized and may require a sponsor to conduct post-marketing clinical trials (Phase 4 clinical trials), which are designed to further assess a drug's safety and effectiveness after NDA approval. The FDA may also place other conditions on approval, including a requirement for a risk evaluation and mitigation strategy ("REMS") to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescribing or dispensing of products. Marketing approval may be withdrawn for non-compliance with REMS or other regulatory requirements, or if problems occur following initial marketing.

Post-approval requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the drug reaches the market. Later discovery of previously unknown problems with a drug may result in restrictions on the drug or even complete withdrawal of the drug from the market. After approval, some types of changes to the approved drug, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP regulations and other laws and regulations.

Any drug product manufactured or distributed by us pursuant to FDA approval will be subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. FDA strictly regulates labeling, advertising, promotion and other types of information regarding approved drugs that are placed on the market, and imposes requirements and restrictions on drug manufacturers, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product for a certain indication or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable governmental requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. The FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds on post-marketing clinical trials, enforcement letters, import refusals, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties.

Expedited development and review programs

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. With regard to a fast track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval.

A product is eligible for priority review if it is intended to treat a serious condition, and if approved, would provide a significant improvement in safety or efficacy compared to currently marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date, as compared to ten months for review of NDAs under its current PDUFA review goals.

In addition, a product may be eligible for accelerated approval. Drugs intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. Drugs receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing trials or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

The Food and Drug Administration Safety and Innovation Act ("FDASIA") established a category of drugs referred to as "breakthrough therapies" that may be eligible to receive breakthrough therapy designation. A sponsor may seek FDA designation of a compound as a "breakthrough therapy" if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.

Fast track designation, priority review and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process. However, even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States or, if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before an NDA is submitted. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are publicly disclosed by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. However, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of one of our compounds for seven years if our compound is determined to be contained within the competitor's product for the same indication or disease, or if a competitor obtains approval of the same drug as defined by the FDA. In addition, if an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity.

Abbreviated New Drug Applications, 505(b)(2) Applications, and Marketing exclusivity

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's drug or an approved method of use of the drug. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the "Orange Book." Drugs listed in the Orange Book can, in turn, be cited by competitors in support of approval of an Abbreviated New Drug Application, or ANDA, or a 505(b)(2) application. In this case, the original NDA (the so-called pioneer drug) is known as the "listed" drug or "reference-listed" drug. An ANDA provides for marketing of a drug that has the same active ingredient and the same strength, route of administration and dosage form as the listed drug and has been shown through testing to be bioequivalent to the listed drug or receives a waiver from bioequivalence testing. ANDA applicants are generally not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug, other than the requirement for bioequivalence testing. Drugs approved in this way are considered therapeutically equivalent, and are commonly referred to as "generic equivalents" to the listed drug. These drugs then generally can be substituted by pharmacists under prescriptions written for the original listed drug.

A 505(b)(2) application is a type of NDA that relies, in part, upon data the applicant does not own and to which it does not have a right of reference. Such applications often are submitted for changes to previously approved drug products, and rely on the FDA's prior findings of safety and effectiveness for a third party's NDA to abbreviate the showings the sponsor of the 505(b)(2) application must make to establish that its product is safe and effective.

The ANDA or 505(b)(2) applicant is required to certify to FDA concerning any patents listed for the referenced approved drug in FDA's Orange Book. Specifically, for each listed patent, the applicant must certify that: (1) the required patent information has not been filed; (2) the listed patent has expired; (3) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patent is invalid, unenforceable or will not be infringed by the new drug. A certification that the new drug will not infringe the already approved drug's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the ANDA or 505(b)(2) applicant does not include a Paragraph IV certification, the ANDA or 505(b)(2) application will not be approved until all of the listed patents claiming the referenced drug have expired, except for any listed patents that only apply to uses of the drug not being sought by the ANDA or 505(b)(2) applicant.

If the ANDA or 505(b)(2) applicant has made a Paragraph IV certification, the applicant must also send notice of a Paragraph IV Notice Letter to the NDA and patent holders once the ANDA or 505(b)(2) application has been accepted for filing by FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV Notice Letter. The filing of a patent infringement lawsuit within 45 days of the receipt of notice of a Paragraph IV Notice Letter automatically prevents FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, modification by a court or a decision in the infringement case that is favorable to the ANDA or 505(b)(2) applicant. As discussed below, the ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the reference-listed drug has expired.

Market exclusivity provisions under the FDCA can delay the submission or approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application ("ANDA"), or an NDA submitted under Section 505(b)(2) (a "505(b)(2) NDA"), submitted by another company for another drug containing the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active ingredient for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials. In addition, orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

United States Patent Term Restoration

Depending upon the timing, duration and specifics of FDA approval of our future product candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit restoration of the patent term of up to five years as compensation for patent term lost during the FDA regulatory review process for a drug that has not been previously approved for commercial marketing. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. The patent-term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Foreign Sales

Sales outside the United States of potential drug compounds we develop will also be subject to foreign regulatory requirements governing human clinical trials and marketing for drugs. The requirements vary widely from country to country, but typically the registration and approval process takes several years and requires significant resources. In most cases, if the FDA has not approved a potential drug compound for sale in the United States, the potential drug compound may be exported for sale outside of the United States, only if it has been approved in any one of the following: the European Union or a country in the European Economic Area (the countries in the European Union and the European Free Trade Association) if the drug or device is marketed in that country or the drug or device is authorized for general marketing in the European Economic Area, Canada, Australia, New Zealand, Japan, Israel, Switzerland and South Africa. There are specific FDA regulations that govern this process.

U.S. coverage and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any compound for which we may seek regulatory approval. Sales in the United States will depend in part on the availability of sufficient coverage and adequate reimbursement from third-party payors, which include government health programs such as Medicare, Medicaid, CHIP, TRICARE and the Veterans Administration, as well as managed care organizations and private health insurers. Prices at which we or our customers seek reimbursement for our therapeutic compounds can be subject to challenge, reduction or denial by payors.

The process for determining whether a payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be available. Additionally, in the United States there is no uniform policy among payors for coverage or reimbursement. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies, but also have their own methods and approval processes. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. If coverage and adequate reimbursement are not available, or are available only at limited levels, successful commercialization of, and obtaining a satisfactory financial return on, any product we develop may not be possible.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for marketing, we may need to conduct expensive studies in order to demonstrate the medical necessity and cost-effectiveness of any products, which would be in addition to the costs expended to obtain regulatory approvals. Third-party payors may not consider our compounds to be medically necessary or cost-effective compared to other available therapies, or the rebate percentages required to secure favorable coverage may not yield an adequate margin over cost or may not enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development. Additionally, we or our collaborators may develop companion diagnostic tests for use with our product candidates. Companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

Fraud and Abuse Laws

Federal and state health care laws and regulations restrict business practices in the biopharmaceutical industry. In the biopharmaceutical industry, there are a number of federal and state health care regulatory requirements that apply to entities, including, but not limited to, the federal and state fraud and abuse laws. These laws include, but are not limited to, anti-kickback and self-referral law, civil false claims act law, criminal false statement law, civil monetary penalty laws, exclusion law, and other civil, criminal, and administrative laws. Health care laws, regulations, and guidance continuously evolve and are thereby subject to constant change.

The Federal Anti-Kickback Statute, 42 U.S.C. § 1320a-7b(b), among other things, prohibits the knowing and willful offer, payment, solicitation or receipt of any form of remuneration, whether directly or indirectly and overtly or covertly in cash or in kind, in return for, or to induce the referral of an individual for the:

- furnishing or arranging for the furnishing of items or services reimbursable in whole or in part under Medicare, Medicaid or other federal healthcare programs; or

- purchase, lease, or order of, or the arrangement or recommendation of the purchasing, leasing, or ordering of any item or service reimbursable in whole or in part under Medicare, Medicaid or other federal healthcare programs.

There are a number of narrow safe harbors to the Federal Anti-Kickback Statute. Such safe harbors permit certain payments and business practices that, although they would otherwise potentially implicate the Federal Anti-Kickback Statute, are not treated as an offense under the same if all of the requirements of the specific applicable safe harbor are met. Actual knowledge of the statute or specific intent to violate it is not required in order for a person or entity to have committed a violation.

The Federal Anti-Kickback Statute applies to certain arrangements with healthcare providers, product end users and other parties, including marketing arrangements and discounts and other financial incentives offered in connection with the sales of our products. Regulatory authorities may determine that certain marketing, pricing, or other activities violate the Federal Anti-Kickback Statute or other applicable laws. Noncompliance with the Federal Anti-Kickback Statute can result in civil, administrative and/or criminal penalties, restrictions on the ability to operate in certain jurisdictions, and exclusion from participation in Medicare, Medicaid or other federal healthcare programs. In addition, non-compliance can result in the need to curtail and/or restructure operations. Any penalties, damages, fines, exclusions, curtailment or restructuring of operations could adversely affect the ability to operate a business, financial condition, and results of operations. A violation of the Federal Anti-Kickback Statute can serve as a false or fraudulent claim for purposes of the civil False Claims Act and the civil monetary penalties statute.

The federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) among other things, enacted numerous provisions that prohibit knowingly and willfully executing, or attempting to execute, a scheme or artifice to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. These provisions include 18 U.S.C. §§ 286, 287, 669, 1035, 1347, and 1518, all as described further below.

The Ethics in Patient Referrals Act, commonly known as the “Stark Law,” 42 U.S.C. § 1395nn, prohibits a physician from making referrals for certain “designated health services” payable by Medicare to an entity in which the physician or an immediate family member of such physician has an ownership or investment interest or with which the physician has entered into a compensation arrangement, unless a statutory exception applies. There are a number of exceptions to the Stark Law. Such exceptions permit certain payments and arrangements that, although they would otherwise potentially implicate the Stark Law, are not treated as a violation under the same if the requirements of the specific exceptions are met. Violation of the Stark Law could result in denial of payment, disgorgement of reimbursements received under a noncompliance arrangement, civil penalties, damages and exclusion from Medicare or other governmental programs. These requirements are highly technical and there can be no guarantee that regulatory authorities will not determine or assert that arrangements are in violation of the Stark Law and do not otherwise meet applicable Stark Law exceptions.

The federal false statements statute, 42 U.S.C. § 1320a-7b(a), prohibits knowingly and willfully falsifying, concealing, or omitting a material fact or making any materially false statement in connection with the delivery of health care benefits, items, or services. Similarly, 18 U.S.C. § 1035 prohibits a person or entity, in any matter involving a health care benefit program, from knowingly or willfully falsifying, concealing, or covering up by any trick, scheme, or device a material fact; making any materially false, fictitious, or fraudulent statements or representations; or making or using any materially false writing or document knowing the same to contain any materially false, fictitious, or fraudulent statement or entry. In addition to criminal penalties, violation of these statutes may result in collateral administrative sanctions, including exclusion from participation in Medicare, Medicaid and other federal health care programs.

18 U.S.C. § 669 prohibits knowingly and willfully embezzling, stealing, or otherwise without authority converting to the use of any person or entity other than the rightful owner, or intentionally misapplying any of the moneys, funds, securities, premiums, credits, property, or other assets of a health care benefit program. In addition to criminal penalties, violation of this statute may result in collateral administrative sanctions, including exclusion from participation in Medicare, Medicaid and other federal health care programs.

The criminal health care fraud statute, 18 U.S.C. § 1347, establishes criminal liability for whoever knowingly and willfully executes, or attempts to execute, a scheme or artifice to defraud any health care benefit program, or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any health care benefit program, in connection with the delivery of or payment for health care benefits, items, or services. In addition to criminal penalties, violation of this statute may result in collateral administrative sanctions, including exclusion from participation in Medicare, Medicaid and other federal health care programs. A person or entity need not have actual knowledge of this law or specific intent to commit a violation of this law.

18 U.S.C. § 1518 establishes criminal liability for whoever willfully prevents, obstructs, misleads, delays or attempts to prevent, obstruct, mislead, or delay the communication of information or records relating to a violation of a Federal health care offense to a criminal investigator. In addition to criminal penalties, violation of this statute may result in collateral administrative sanctions, including exclusion from participation in Medicare, Medicaid and other federal health care programs.

18 U.S.C. § 286 establishes criminal liability for whoever enters into any agreement, combination, or conspiracy to defraud the United States, or any department or agency thereof, by obtaining or aiding to obtain the payment or allowance of any false, fictitious or fraudulent claim. In addition to criminal penalties, violation of this statute may result in collateral administrative sanctions, including exclusion from participation in Medicare, Medicaid and other federal health care programs.

18 U.S.C. § 287 establishes criminal liability for whoever knowingly makes or presents a false, fictitious or fraudulent claim to the United States Government, including any department or agency thereof. In addition to criminal penalties, violation of this statute may result in collateral administrative sanctions, including exclusion from participation in Medicare, Medicaid and other federal health care programs.

The Federal False Claims Act, 31 U.S.C. § 3729, et seq., provides, in part, that the federal government—or a private party on behalf of the government—may bring a lawsuit against any person whom it believes has knowingly presented, or caused to be presented, a false or fraudulent claim for payment, or who has made a false statement or used a false record to get a claim paid or to avoid, decrease or conceal an obligation to pay money to the federal government or who has knowingly retained an overpayment. Knowledge under the Federal False Claims Act means actual knowledge, deliberate indifference, or reckless disregard. In addition, amendments in 1986 to the Federal False Claims Act have made it easier for private parties to bring whistleblower lawsuits against companies.

The civil monetary penalties law, 42 U.S.C. § 1320a-7a, provides, in part, that the federal government may seek civil monetary penalties against any person who presents or causes to be presented claims to a Federal health care program that the person knows or should know is for an item or services that was not provided as claimed or is false or fraudulent, or the person has made a false statement or used a false record to get a claim paid. The federal government may also seek civil monetary penalties for a wide variety of other conduct, including offering remuneration to influence a Medicare or Medicaid beneficiary's selection of providers and violations of the Federal Anti-Kickback Statute.

Violations of the Federal False Claims Act and/or the Civil Monetary Penalties Law can result in penalties ranging from $12,537 to $25,076 for each false claim violation of the Federal False Claims Act and varying amounts based on the type of violation of the Civil Monetary Penalties Law, plus up to three times the amount of damages that the federal government sustained. In addition, the federal government may also seek exclusion from participation in all federal health care programs.

42 U.S.C. Section 1320a-7 provides that individuals and entities can be mandatorily or permissively excluded from participation in federal health care programs. The grounds for mandatory exclusion include, but are not limited to, conviction for a criminal offense related to the delivery of an item or service reimbursed under a federal or state health care program, and a conviction related to health care fraud. The grounds for permissive exclusion include, but are not limited to, criminal offenses relating to fraud inside and outside of health care, convictions related to obstruction of an investigation or audit, and/or failure to disclose certain required information. Exclusion from federal health care programs—whether mandatory or permissive—may mean that our customers may not be able to get reimbursed by federal and/or state health care programs for use or dispensing of our products .

State Fraud and Abuse Provisions

Many states have also adopted some form of anti-kickback and anti-referral laws and false claims acts and civil monetary penalties and other fraud and abuse provisions that apply regardless of payer, in addition to items and services reimbursed under Medicaid and other state programs. A determination of liability under such laws could result in fines, penalties, and exclusion, as well as restrictions on the ability to operate in these jurisdictions.

Corporate liability can be present as a result of the illegal activities of employees, representatives, contractors, collaborators, agents, subsidiaries, or affiliates, even if they were not explicitly authorized. There can be no assurance that all employees, representatives, contractors, collaborators, agents, subsidiaries or affiliates will comply with the foregoing laws at all times. Violation of the aforementioned and other laws could result in whistleblower complaints, investigations, sanctions, settlements, prosecution, government oversight and reporting, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions or other administrative remedies, suspension and/or debarment from contracting with certain governments or other persons, the loss of privileges, reputational harm, contract damages, adverse media coverage and other collateral consequences. In addition, corporate directors, officers, employees, and other representatives who engage in violations of these and other laws may face imprisonment, fines, and penalties. If any subpoenas or investigations are launched, or governmental or other sanctions are imposed, or if a company does not prevail in any possible civil or criminal litigation, business, financial condition, and results of operations could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense costs and other professional fees. Enforcement actions and sanctions could further harm business, financial condition, and results of operations. Any of the consequences contained in this paragraph and section could adversely affect the ability to operate the business, financial condition, and the results of operations.

Sunshine Act

The Sunshine Act requires manufacturers of products reimbursed by Medicare, Medicaid or the Children's Health Insurance Program ("CHIP") to collect and annually report detailed data to the Centers for Medicare and Medicaid Services ("CMS") regarding payments or other transfers of value to physicians, certain other health care providers (such as physicians assistants and nurse practitioners), and teaching hospitals ("covered recipients"), as well as any ownership or investment interest held by physicians and their immediate family members. The reporting data must be accompanied by an attestation as to the accuracy of the data and failure to timely and accurately submit required information may result in civil monetary penalties.

Health Insurance Portability and Accountability Act

Besides enacting the program integrity provisions described above, HIPAA, also created a new set of privacy and security requirements. As amended by the Health Information Technology for Economic and Clinical Health Act, and implementing regulations thereunder, HIPAA requires certain healthcare providers, health plans and healthcare clearinghouses who conduct specified electronic healthcare transactions ("covered entities"), as well as their independent contractors and agents who conduct certain activities involving protected health information on their behalf ("business associates") to comply with enumerated requirements relating to the privacy, security and transmission of protected health information. Failure to comply with HIPAA can result in corrective action, as well as civil fines and penalties and government oversight. Among other changes, HITECH made HIPAA security standards directly applicable to business associates, increased the tiered civil and criminal fines and penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file actions to enforce HIPAA. Further, the breach notification rule implemented under HITECH requires covered entities to notify affected individuals, the U.S. Department of Health and Human Services Office of Civil Rights ("OCR"), the agency that enforces HIPAA, and for breaches affecting more than 500 individuals, the media, of any breaches of unsecured protected health information. HIPAA does not create a private right of action for individuals, though individuals may submit complaints related to HIPAA to OCR.

Legislative Activities Aimed at Controlling Drug Costs

In the United States, there have been, and continue to be proposed and enacted legislation at the federal and state levels designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. For example, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the U.S. Department of Health and Human Services ("HHS") released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the Inflation Reduction Act ("IRA") passed on August 16, 2022. The IRA, among other things, (1) directs HHS to negotiate the price of certain highly-utilized single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report within 90 days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Research and Development Expenses

Historically, a significant portion of our operating expenses has related to research and development. See our Consolidated Financial Statements contained elsewhere in this Annual Report for costs and expenses related to research and development, and other financial information for fiscal years 2022, 2021 and 2020.

Scientific Advisors

We are advised by scientists and physicians with experience relevant to our Company and our product candidates. Our scientific advisors include clinicians and scientists who are affiliated with a number of highly regarded medical institutions.

Employees

We currently have approximately thirty-eight full-time employees, and we retain several independent contractors on a regular or as-needed basis. We believe that we have good relations with our employees.

Available Information

Our internet website address is www.anavex.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to section 13(a) or 15(d) of the Exchange Act are available free of charge through our website. We include our website address in this report only as an inactive textual reference and do not intend it to be an active link to our website. The contents of our website are not incorporated into this report.

ITEM 1A. RISK FACTORS

In addition to other information in this Annual Report on Form 10-K, the following risk factors should be carefully considered in evaluating our business because such factors may have a significant impact on our business, operating results, liquidity and financial condition. As a result of the risk factors set forth below, actual results could differ materially from those projected in any forward-looking statements. Additional risks and uncertainties not presently known to us, or that we currently consider to be immaterial, may also impact our business, operating results, liquidity and financial condition. If any such risks occur, our business, operating results, liquidity and financial condition could be materially affected in an adverse manner. Under such circumstances, the trading price of our securities could decline, and you may lose all or part of your investment.

Risks Related to our Company

We have had a history of losses and no revenue, which raises a risk regarding our ability to continue as a going concern in the future.

Since inception through September 30, 2022, we have accumulated a deficit of approximately $246 million. We can offer no assurance that we will ever operate profitably or that we will generate positive cash flow in the future. To date, we have not generated any revenues from our operations. Our history of losses and no revenues creates a greater risk of our continued ability to continue as a going concern in the future. As a result, our management expects the business to continue to experience negative cash flows for the foreseeable future and cannot predict when, if ever, our business might become profitable. We will need to raise additional funds, and such funds may not be available on commercially acceptable terms, if at all. If we are unable to raise funds on acceptable terms, we may not be able to execute our business plan, take advantage of future opportunities, or respond to competitive pressures or unanticipated requirements. This may seriously harm our business, financial condition and results of operations.

We are an early clinical stage pharmaceutical research and development company and may never be able to successfully develop marketable products or generate any revenue. We have a very limited relevant operating history upon which an evaluation of our performance and prospects can be made. There is no assurance that our future operations will result in profits. If we cannot generate sufficient revenues, we may suspend or cease operations.

We are an early clinical stage company and have not generated any revenues to date and have no operating history. Moreover, we cannot be certain that our research and development efforts will be successful or, if successful, that our potential drug compounds will ever be approved for sales to pharmaceutical companies or generate commercial revenues. We have no relevant operating history upon which an evaluation of our performance and prospects can be made. We are subject to all of the business risks associated with a new enterprise, including, but not limited to, risks of unforeseen capital requirements, failure of potential drug compounds either in non-clinical testing or in clinical trials, failure to establish business relationships and competitive disadvantages against larger and more established companies. If we fail to become profitable, we may suspend or cease operations.

We will need additional funding and may be unable to raise additional capital when needed, which would force us to delay, reduce or eliminate our research and development activities.

To date, we have funded our operations primarily through private placement of our equity securities, grants and our "at the market offering" in connection with an Amended and Restated Sales Agreement, dated May 1, 2020, with Cantor Fitzgerald & Co. and SVB Leerink LLC (the "Sales Agents"), pursuant to which we may offer and sell shares of common stock registered under an effective registration statement from time to time through the Sales Agents. We will need to raise additional funding and the current economic conditions may have a negative impact on our ability to raise additional needed capital on terms that are favorable to our Company or at all. We may not be able to generate significant revenues for several years, if at all. Until we can generate significant revenues, if ever, we expect to satisfy our future cash needs through equity or debt financing. We cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available, we may be required to delay, reduce the scope of, or eliminate one or more of our research and development activities.

Risks Related to our Business

Even if we are able to develop our potential drug compounds, we may not be able to receive regulatory approval, or if approved, we may not be able to generate significant revenues or successfully commercialize our products, which will adversely affect our financial results and financial condition and we will have to delay or terminate some or all of our research and development plans which may force us to cease operations.

All of our potential drug compounds are exclusively focused on SIGMAR1 which has not previously been the subject of any approved drug products and will require extensive additional research and development, including non-clinical testing and clinical trials, as well as regulatory approvals, before we can market them. In particular, human therapeutic products are subject to rigorous non-clinical and clinical testing and other approval procedures of the FDA and similar regulatory authorities in other countries. Various federal statutes and regulations also govern or influence testing, manufacturing, safety, labeling, storage, and record-keeping related to such products and their marketing. We cannot predict if or when any of the potential drug compounds we intend to develop will be approved for marketing. There are many reasons that we may fail in our efforts to develop our potential drug compounds. These include:

- the possibility that non-clinical testing or clinical trials may show that our potential drug compounds are ineffective and/or cause harmful side effects;
- regulators may not authorize us to commence or continue a clinical trial or may impose a clinical hold or may limit the conduct of a clinical trial through the imposition of a partial clinical hold;
- the number of patients required for clinical trials for our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate or the duration of these clinical trials may be longer than we anticipate;

- our third-party contractors, including investigators, may fail to meet their contractual obligations to us in a timely manner, or at all, or may fail to comply with regulatory requirements;
- our potential drug compounds may prove to be too expensive to manufacture or administer to patients;
- our potential drug compounds may fail to receive necessary regulatory approvals from the United States Food and Drug Administration or foreign regulatory authorities in a timely manner, or at all;
- even if our potential drug compounds are approved, we may not be able to produce them in commercial quantities or at reasonable costs;
- even if our potential drug compounds are approved, they may not achieve commercial acceptance;
- regulatory or governmental authorities may apply restrictions to any of our potential drug compounds, which could adversely affect their commercial success; and
- the proprietary rights of other parties may prevent us or our potential collaborative partners from marketing our potential drug compounds.

If we fail to develop our potential drug compounds, our financial results and financial condition will be adversely affected, we will have to delay or terminate some or all of our research and development plans and may be forced to cease operations.

Our research and development plans will require substantial additional future funding which could impact our operations and financial condition.

It will take several years before we can develop potentially marketable products, if at all. Our research and development plans will require substantial additional capital, arising from costs to:

- conduct research, non-clinical testing and human clinical trials;
- establish pilot scale and commercial scale manufacturing processes and facilities; and
- establish and develop quality control, regulatory, marketing, sales, finance and administrative capabilities to support these programs.

Our future operating and capital needs will depend on many factors, including:

- the pace of scientific progress in our research and development programs and the magnitude of these programs;
- the scope and results of pre-clinical testing and human clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the time and costs involved in preparing, filing, prosecuting, securing, maintaining and enforcing patents;
- competing technological and market developments;
- our ability to establish additional collaborations;
- changes in our existing collaborations;
- the cost of manufacturing scale -up; and
- the effectiveness of our commercialization activities.

We base our outlook regarding the need for funds on many uncertain variables. Such uncertainties include the success of our research initiatives, regulatory approvals, the timing of events outside our direct control such as negotiations with potential strategic partners and other factors. Any of these uncertain events can significantly change our cash requirements as they determine such one-time events as the receipt or payment of major milestones and other payments.

Additional funds may be required to support our operations and if we are unable to obtain them on favorable terms, we may be required to cease or reduce certain further research and development programs of our drug product platform, sell some or all our intellectual property, merge with another entity or scale back operations.

If we or any companion diagnostic collaborator of ours are unable to successfully develop and obtain regulatory approval for companion diagnostic tests for our drug candidates, or experience significant delays in doing so, we may not realize the commercial potential of our drug candidates.

We analyze genomic data from clinical trials to identify biomarkers, which we use in the analysis of our clinical trials.

Identification of these patients will require the use and development of companion diagnostics. According to the FDA's 2014 guidance document on In Vitro Companion Diagnostic Devices, for novel therapeutic products that depend on the use of a diagnostic test and where the diagnostic device could be essential for the safe and effective use of the corresponding therapeutic product, the premarket application for the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic.

We do not have experience or capabilities in developing or commercializing diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a drug candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our future collaborators may encounter difficulties in developing, obtaining regulatory approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our drug candidates, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we are unable to successfully develop companion diagnostics for our drug candidates, or experience delays in doing so, the development of these drug candidates may be adversely affected, these drug candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these therapeutics that have or may obtain marketing approval. We may not be able to enter into arrangements with another diagnostic company to develop and obtain regulatory approval for of an alternative diagnostic test for use in connection with the development and commercialization of our drug candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our therapeutic candidates or therapeutics.

Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and will likely require separate regulatory approval prior to commercialization. If we or third parties are unable to successfully develop companion diagnostics for our drug candidates, or experience delays in doing so:

- the development of these drug candidates may be delayed because it may be difficult to identify patients for enrollment in our clinical trials in a timely manner;
- these drug candidates may not receive marketing approval if their safe and effective use depends on a companion diagnostic; and
- we may not realize the full commercial potential of these drug candidates that receive marketing approval if, among other reasons, we are unable to appropriately identify patients or types of tumors targeted by these drug candidates.

Even if our drug candidates and any associated companion diagnostics are approved for marketing, the need for companion diagnostics may slow or limit adoption of our drug candidates. Our drug candidates may be perceived negatively compared to alternative treatments that do not require the use of companion diagnostics, either due to the additional cost of the companion diagnostic or the need to complete additional prior to administering our drug candidates.

If any of these events were to occur, our business and growth prospects would be harmed materially.

All but one of our clinical trials to date have been conducted outside the United States, and the FDA and other foreign regulatory authorities may not accept data from such trials.

The acceptance of study data from clinical trials conducted outside the United States by the FDA may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for regulatory approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any other foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

We have received Fast Track designation for one of our compounds and may seek such designation or breakthrough therapy and priority review for other compounds in the future. Fast Track designation or breakthrough therapy designation may not actually lead to a faster FDA review and approval process.

For some of our compounds, including ANAVEX ®2-73, we hope to benefit from the FDA's fast track and priority review programs. In February 2020, the FDA granted Fast Track designation for the ANAVEX®2-73 clinical development program for the treatment of Rett syndrome. Programs with Fast Track designation may benefit from early and frequent communications with the FDA, potential priority review and the ability to submit a rolling application for regulatory review. Fast Track designation applies to both the product candidate and the specific indication for which it is being studied. If any of our compounds receive Fast Track designation but do not continue to meet the criteria for Fast Track designation, or if our clinical trials are delayed, suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply, we will not receive the benefits associated with the Fast Track program. Furthermore, Fast Track designation does not change the standards for approval. The receipt of Fast Track designation for a compound may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if any product candidate qualifies for Fast Track designation, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures.

Under FDA policies, a compound is eligible for priority review, or review within a six-month time frame from the time a complete NDA is accepted for filing, if the compound provides a significant improvement compared to marketed drugs in the treatment, diagnosis or prevention of a disease. The FDA determines whether a drug qualifies for Priority Review after an NDA for such drug is submitted to the FDA. Therefore, until NDAs are submitted for our compounds, we cannot be assured that they will be granted Priority Review. Additionally, even if Priority Review is granted for one of our compounds, the FDA does not always meet its six-month PDUFA goal date for Priority Review and the review process is often extended by FDA requests for additional information or clarification.

We may seek Breakthrough Therapy designation for one or more of our current or future compounds. Designation as a Breakthrough Therapy is largely within the discretion of the FDA. Accordingly, even if we believe that a compound meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to candidate products considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by the FDA. In addition, even if one or more compounds qualify as breakthrough therapies, the FDA may later decide that the product no longer meets the conditions for qualification and revoke the designation.

Fast track or breakthrough therapy designation for our compounds may not actually lead to a faster review process, and a delay in the review process or in the approval of our compounds will delay revenue from their potential sales and will increase the capital necessary to fund these compound development programs.

We have received orphan drug designation for several of our compounds, but we may be unable to maintain any benefits associated with orphan drug designation, including market exclusivity.

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition or for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for a disease or condition will be recovered from sales in the United States for that drug. If a product that has orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full NDA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity.

We have received orphan drug designation for several of our compounds, but we may not be able to obtain or maintain orphan drug exclusivity in the United States for hose compounds. We may not be the first to obtain marketing approval of any compound for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek FDA marketing approval for an indication broader than the orphan designated indication. Additionally, any compound with orphan drug designation may lose such designation if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, others may obtain orphan drug exclusivity for products addressing the same diseases or conditions as products we are developing, thus limiting our ability to compete in the markets addressing such diseases or conditions for a significant period of time. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process or entitles the product candidate to priority review.

If we fail to demonstrate efficacy in our non-clinical studies and clinical trials our future business prospects, financial condition and operating results will be materially adversely affected.

The success of our research and development efforts will be greatly dependent upon our ability to demonstrate potential drug compound efficacy in non-clinical studies, as well as in clinical trials. Non-clinical studies involve testing potential drug compounds in appropriate non-human disease models to demonstrate efficacy and safety. Regulatory agencies evaluate these data carefully before they will approve clinical testing in humans. If certain non-clinical data reveals potential safety issues or the results are inconsistent with an expectation of the potential drug compound's efficacy in humans, the regulatory agencies may require additional more rigorous testing before allowing human clinical trials. This additional testing will increase program expenses and extend timelines. We may decide to suspend further testing on our potential drug compounds if, in the judgment of our management and advisors, the non-clinical test results do not support further development.

Moreover, success in non-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and non-clinical testing. The clinical trial process may fail to demonstrate that our potential drug compounds are safe for humans and effective for indicated uses. This failure would cause us to abandon a drug candidate and may delay development of other potential drug compounds. Any delay in, or termination of, our non-clinical testing or clinical trials will delay the filing of an IND and NDA with the FDA or the equivalent applications with pharmaceutical regulatory authorities outside the United States and, ultimately, our ability to commercialize our potential drug compounds and generate product revenues. In addition, we expect that our early clinical trials will involve small patient populations. Because of the small sample size, the results of these early clinical trials may not be indicative of future results. Also, the IND process may be extremely costly and may substantially delay the development of our potential drug compounds. Moreover, positive results of non-clinical tests will not necessarily indicate positive results in subsequent clinical trials.

Following successful non-clinical testing, potential drug compounds will need to be tested in a clinical development program to provide data on safety and efficacy prior to becoming eligible for product approval and licensure by regulatory agencies. From the first human trial through to regulatory approval can take many years and 10-12 years is not unusual for certain compounds.

If any of our future clinical development potential drug compounds become the subject of problems, our ability to sustain our development programs will become critically compromised. For example, efficacy or safety concerns may arise, whether or not justified, that could lead to the suspension or termination of our clinical programs. Examples of problems that could arise include, among others:

- efficacy or safety concerns with the potential drug compounds, even if not justified;
- manufacturing difficulties or concerns;
- regulatory proceedings subjecting the potential drug compounds to potential recall;
- publicity affecting doctor prescription or patient use of the potential drug compounds;
- pressure from competitive products; or
- introduction of more effective treatments.

Each clinical phase is designed to test attributes of the drug and problems that might result in the termination of the entire clinical plan can be revealed at any time throughout the overall clinical program. The failure to demonstrate efficacy in our clinical trials would have a material adverse effect on our future business prospects, financial condition and operating results.

If we do not obtain the support of qualified scientific collaborators, our revenue, growth and profitability will likely be limited, which would have a material adverse effect on our business.

We will need to establish relationships with leading scientists and research institutions. We believe that such relationships are pivotal to establishing products using our technologies as a standard of care for various indications. Additionally, although in discussion, there is no assurance that our current research partners will continue to work with us or that we will be able to attract additional research partners. If we are not able to establish scientific relationships to assist in our research and development, we may not be able to successfully develop our potential drug compounds. If this happens, our business will be adversely affected.

We may not be able to develop, market or generate sales of our products to the extent anticipated. Our business may fail and investors could lose all their investment in our Company.

Assuming that we are successful in developing our potential drug compounds and receiving regulatory clearances to market our products, our ability to successfully penetrate the market and generate sales of those products may be limited by a number of factors, including the following:

- If our competitors receive regulatory approvals for and begin marketing similar products in the United States, the European Union, Japan and other territories before we do, greater awareness of their products as compared to ours will cause our competitive position to suffer;
- Information from our competitors or the academic community indicating that current products or new products are more effective or offer compelling other benefits than our future products could impede our market penetration or decrease our future market share; and
- The pricing and reimbursement environment for our future products, as well as pricing and reimbursement decisions by our competitors and by payers, may have an effect on our revenues.

If this happens, our business will be adversely affected.

None of our potential drug compounds may reach the commercial market for a number of reasons and our business may fail.

Successful research and development of pharmaceutical products is high risk. Most products and development candidates fail to reach the market. Our success depends on the discovery of new drug compounds that we can commercialize. It is possible that our products may never reach the market for a number of reasons. They may be found ineffective or may cause harmful side-effects during non-clinical testing or clinical trials or fail to receive necessary regulatory approvals. We may find that certain products cannot be manufactured at a commercial scale and, therefore, they may not be economical to produce. Our potential products could also fail to achieve market acceptance or be precluded from commercialization by proprietary rights of third parties. Our patents, patent applications, trademarks and other intellectual property may be challenged, and this may delay or prohibit us from effectively commercializing our products. Furthermore, we do not expect our potential drug compounds to be commercially available for a number of years, if at all. If none of our potential drug compounds reach the commercial market, our business will likely fail and investors will lose all of their investment in our Company. If this happens, our business will be adversely affected.

If our competitors succeed in developing products and technologies faster or that are more effective or with a better profile than our own, or if scientific developments change our understanding of the potential scope and utility of our potential products, then our technologies and future products may be rendered undesirable or obsolete.

We face significant competition from industry participants that are pursuing technologies in similar disease states to those that we are pursuing and are developing pharmaceutical products that are competitive with our products. Nearly all of our industry competitors have greater capital resources, larger overall research and development staffs and facilities, and a longer history in drug discovery and development, obtaining regulatory approval and pharmaceutical product manufacturing and marketing than we do. With these additional resources, our competitors may be able to respond to the rapid and significant technological changes in the biotechnology and pharmaceutical industries faster than we can. Our future success will depend in large part on our ability to maintain a competitive position with respect to these technologies. Rapid technological development, as well as new scientific developments, may result in our products becoming obsolete before we can recover any of the expenses incurred to develop them. For example, changes in our understanding of the appropriate population of patients who should be treated with a targeted therapy like we are developing may limit the drug's market potential if it is subsequently demonstrated that only certain subsets of patients should be treated with the targeted therapy.

We have advanced our research and development efforts on the treatment of neurodegenerative and central nervous system, or CNS, disorders, a field that has seen very limited success in product development.

We have advanced our research and development efforts on addressing neurodegenerative, neurodevelopmental and CNS disorders. Collectively, efforts by pharmaceutical companies in the field of neurodegenerative, neurodevelopmental and CNS disorders have seen very limited successes in product development. The development of neurodegenerative and CNS therapies presents unique challenges, including an imperfect understanding of the biology, the presence of the blood brain barrier, or BBB, that can restrict the flow of drugs to the brain, a frequent lack of translatability of preclinical study results in subsequent clinical trials and dose selection, and the product candidate having an effect that may be too small to be detected using the outcome measures selected in clinical trials or if the outcomes measured do not reach statistical significance.

Our reliance on third parties, such as university laboratories, contract manufacturing organizations and contract or clinical research organizations, may result in delays in completing, or a failure to complete, non-clinical testing or clinical trials if they fail to perform under our agreements with them or non-compliance with regulations.

In the course of product development, we may engage university laboratories, other biotechnology companies or contract or clinical manufacturing organizations to manufacture drug material for us to be used in non-clinical and clinical testing and contract research organizations to conduct and manage non-clinical studies and clinical trials. If we engage these organizations to help us with our non-clinical and clinical programs, many important aspects of this process have been and will be out of our direct control. If any of these organizations we may engage in the future fail to perform their obligations under our agreements with them or fail to perform non-clinical testing and/or clinical trials in a satisfactory manner, we may face delays in completing our clinical trials, as well as commercialization of any of our potential drug compounds. Furthermore, any loss or delay in obtaining contracts with such entities may also delay the completion of our clinical trials, regulatory filings and the potential market approval of our potential drug compounds.

In addition, any of these third parties may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of any regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; or laws that require the reporting of financial information or data accurately. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations.

If we fail to compete successfully with respect to partnering, licensing, mergers, acquisitions, joint venture and other collaboration opportunities, we may be limited in our ability to research and develop our potential drug compounds.

Our competitors compete with us to attract established biotechnology and pharmaceutical companies or organizations for partnering, licensing, mergers, acquisitions, joint ventures or other collaborations. Collaborations include contracting with academic research institutions for the performance of specific scientific testing. If our competitors successfully enter into partnering arrangements or license agreements with academic research institutions, we will then be precluded from pursuing those specific opportunities. Since each of these opportunities is unique, we may not be able to find a substitute. Other companies have already begun many drug development programs, which may target diseases that we are also targeting, and have already entered into partnering and licensing arrangements with academic research institutions, reducing the pool of available opportunities.

Universities and public and private research institutions also compete with us. While these organizations primarily have educational or basic research objectives, they may develop proprietary technology and acquire patent applications and patents that we may need for the development of our potential drug compounds. In some instances, we will attempt to license this proprietary technology, if available. These licenses may not be available to us on acceptable terms, if at all. If we are unable to compete successfully with respect to acquisitions, joint venture and other collaboration opportunities, we may be limited in our ability to develop new products.

The use of any of our products in clinical trials may expose us to liability claims, which may cost us significant amounts of money to defend against or pay out, causing our business to suffer.

The nature of our business exposes us to potential liability risks inherent in the testing, manufacturing and marketing of our products. We currently have one drug compound in clinical trials, however, when any of our products enter clinical trials or become marketed products, they could potentially harm people or allegedly harm people possibly subjecting us to costly and damaging product liability claims. Some of the patients who participate in clinical trials are already ill when they enter a trial or may intentionally or unintentionally fail to meet the exclusion criteria. The waivers we obtain may not be enforceable and may not protect us from liability or the costs of product liability litigation. Although we intend to obtain product liability insurance, which we believe is adequate, we are subject to the risk that our insurance will not be sufficient to cover claims. The insurance costs along with the defense or payment of liabilities above the amount of coverage could cost us significant amounts of money and management distraction from other elements of the business, causing our business to suffer.

If we are unable to safeguard against security breaches with respect to our information systems, our business may be adversely affected.

In the course of our business, we gather, transmit and retain confidential information through our information systems. Although we endeavor to protect confidential information through the implementation of security technologies, processes and procedures, it is possible that an individual or group could defeat security measures and access sensitive information about our business and employees. Any misappropriation, loss or other unauthorized disclosure of confidential information gathered, stored or used by us could have a material impact on the operation of our business, including damaging our reputation with our employees, third parties and investors. We could also incur significant costs implementing additional security measures and organizational changes, implementing additional protection technologies, training employees or engaging consultants. In addition, we could incur increased litigation as a result of any potential cyber-security breach. We are not aware that we have experienced any material misappropriation, loss or other unauthorized disclosure of confidential or personally identifiable information as a result of a cyber-security breach or other act, however, a cyber-security breach or other act and/or disruption to our information technology systems could have a material adverse effect on our business, prospects, financial condition or results of operations.

Even if we receive regulatory approval for one or more compounds, we will be subject to continuing regulatory obligations and ongoing regulatory review, which may result in significant additional expense. Additionally, our compounds, if approved, could be subject to labeling and other restrictions on marketing or withdrawal from the market, and we may be subject to penalties, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our compounds, when and if any of them are approved.

Following potential approval of any our compounds, the FDA may impose significant restrictions on a drug's indicated uses or marketing or require potentially costly and time-consuming post-approval studies, post-market surveillance or clinical trials to monitor the safety and efficacy of the drug. The FDA may also require a Risk Evaluation and Mitigation Strategy ("REMS") as a condition of approval of one or more of our compounds, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use of the drug. Additional REMS elements may include restricted distribution methods, patient registries and other risk minimization tools.

In addition, if the FDA or a comparable foreign regulatory authority approves one or more of our compounds, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for the approved drug will be subject to additional and potentially extensive ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, establishment registration, as well as continued compliance with cGMPs and GCP requirements for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our products, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, restitutions, disgorgement of profits or revenues, warning letters, untitled letters or holds on clinical trials;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- product seizure or detention, or refusal to permit the import or export of our products;
- injunctions or the imposition of civil or criminal penalties; and
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals.

The occurrence of any event or penalty described above may limit our ability to commercialize our compounds and generate revenue, and could require us to expend significant time and resources in response or generate negative publicity.

If any of our compounds are approved, our product labeling, advertising and promotion will also be subject to regulatory requirements and ongoing regulatory review. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a drug may not be promoted for uses that are not approved by the FDA as reflected in the drug's approved labeling. If we receive marketing approval for a compound, physicians may nevertheless lawfully prescribe it to their patients in a manner that is inconsistent with the approved label. While the FDA recently clarified that mere knowledge that a physician is prescribing an approved drug for off label use is not sufficient to constitute unlawful off-label promotion, if we are found to have actively promoted such off label uses, we may become subject to significant liability under the FDCA. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. Additionally, promotion for off label uses could result in significant liability under the False Claims Act. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

The FDA's and other regulatory authorities' policies are subject to change at any time, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our compounds. If we are unable to timely adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance post-marketing, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

Finally, we cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. It is difficult to predict how any such legislative, administrative or executive actions will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these legislative or executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

The COVID-19 coronavirus could adversely impact our business, including our clinical trials, and financial condition.

In December 2019, a novel strain of coronavirus, COVID-19, was reported to have surfaced in Wuhan, China. Since then, the COVID-19 coronavirus has spread to multiple countries, including the United States, Australia and European and Asia-Pacific countries, including countries in which we have planned or active clinical trial sites. As the COVID-19 coronavirus continues to spread around the globe, we may experience disruptions that could potentially impact our business and clinical trials.

The extent to which the COVID-19 coronavirus may impact our future business operations, including our clinical trials, and financial condition will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. Moreover, to the extent the COVID-19 pandemic adversely affects our business, financial condition and results of operations, it may also have the effect of heightening many of the other risks described in this "Risk Factors" section.

We receive Australian government research and development income tax incentive refunds. If our research and development expenditures are not deemed to be eligible for the refund, proposed modifications to the tax incentive program are enacted, or the tax incentive program is discontinued by the Australian government, it could have a negative effect on our future cash flows and the funding of future research and development projects.

Our subsidiary, Anavex Australia Pty Ltd., is incorporated in Australia where we are currently engaged in research and development activities for ANAVEX®2-73 and ANAVEX®3-71. Our subsidiary is eligible to participate in the Australian Federal Government's Research and Development Tax Incentive program, under which the government provides a cash refund for a portion of eligible research and development expenditures (currently 43.5% to 48.5% depending on the entity's corporate tax rate) by small Australian entities, which are defined as Australian entities with less than $20 million (Australian) in revenue.

The Research and Development Tax Incentive refund is offered by the Australian federal government for eligible research and development purposes based on the filing of an annual application. As part of this program, our subsidiary applied for and received cash refunds from the Australian Taxation Office, or the ATO, for a percentage of the research and development costs expended by our subsidiary in Australia. Since the fiscal year ended September 30, 2015, we have been receiving Research and Development Tax Incentive refunds related to research and development expenditures made.

Certain research and development expenses incurred outside of Australia are also eligible for the Australian research and development tax incentive program, provided we obtain an Advance Overseas Finding from AusIndustry, a division of the Australian Government's Department of Industry, Innovation and Science ("AusIndustry"). To receive an Advance Overseas Finding, the expenses must have been for eligible research and development activities, as determined by AusIndustry, and the expenditures must have a scientific link to the Australian activities, be unable to be conducted in Australia and the total actual and reasonably anticipated overseas costs must be expected to be less than the total actual and reasonably anticipated expenditures for activities conducted within Australia, as determined by AusIndustry at the time of application for an Advance Overseas Finding ("OSF").

This OSF binds both AusIndustry and the Commissioner of Taxation for three income years. However, for compliance purposes, specific issue guidance jointly issued by AusIndustry and the ATO in 2014 provides that an OSF can apply for the duration of the overseas activity provided the activities are not new or materially different then the activities described in the OSF. Currently, the Company is outside of the binding three-year period with respect to OSF applicable to some of its programs being claimed in Australia.

To the extent that some or all of our research and development expenditures are deemed to be "ineligible," then our refunds may decrease or be eliminated. In addition, the Australian government may in the future modify the requirements of, reduce the amounts of the refunds available under, or discontinue the Research and Development Tax Incentive program. Any such change to our anticipated refunds or change to the Research and Development Tax Incentive program would have a negative effect on our future cash flows.

A variety of risks are associated with operating our business internationally which could materially adversely affect our business.

We are presently conducting clinical development solely in Australia, United Kingdom, The Netherlands, Germany and Canada and may choose to conduct additional international and U.S. clinical trials in the future. Additionally, while we have not taken any steps to enter into any non-U.S. markets, we may do so in the future. Accordingly, we are subject to risks related to operating in foreign countries, including:

- different standards of care in various countries that could complicate the evaluation of our product candidates;
- different United States and foreign drug import and export rules;
- reduced protection for intellectual property rights in certain countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad;
- compliance with the FCPA and other anti-corruption and anti-bribery laws;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- different payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;
- potential liability resulting from development work conducted by foreign partners;
- business interruptions resulting from natural disasters, outbreaks of contagious diseases, such as COVID-19, or geopolitical actions, including war and terrorism, or systems failure including cybersecurity breaches; and
- compliance with evolving and expansive foreign regulatory requirements, including data privacy laws (such as the GDPR).

Additionally, in connection with the ongoing conflict between Russia and Ukraine, the U.S. government and European Union countries have imposed enhanced export controls on certain products and sanctions on certain industry sectors and parties in Russia. The U.S. government has also indicated it will consider imposing additional sanctions and other similar measures in the near future. Although we do not currently conduct any clinical trials in Russia or Ukraine, further escalation of geopolitical tensions could have a broader impact that expands into other markets where we do business or conduct certain research and development operations, which could adversely affect our business, our supply chain for our product candidates, our collaborators or our ability to carry out our clinical trials.

Our ability to use our net operating loss ("NOL") carryforwards and certain tax credit carryforwards may be subject to limitation.

As of September 30, 2022, we had $123.4 million of U.S. federal and $199.0 million of state and local NOL carryforwards. We had approximately $10.6 million of NOL carryforwards in Australia as of the same period. Our NOL carryforwards are subject to review and possible adjustment by the U.S. and state tax authorities. In addition, under Sections 382 and 383 of the Code and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and research and development credits to offset its post-change income may be limited. This could limit the amount of NOLs or research and development credit carryforwards that we can utilize annually to offset future taxable income or tax liabilities. Subsequent ownership changes and changes to the U.S. tax rules in respect of the utilization of NOLs and research and development credits carried forward may further affect the limitation in future years. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

We conducted a Section 382 study during the year ended September 30, 2021 and determined that, during the year ended September 30, 2015, there was a change in ownership which resulted in $25.8 million of federal NOLs being subject to an annual limitation. During the year ended September 30, 2021, we reduced our federal NOLs by $12.1 million and our research and development tax credit carryforwards by $0.8 million, which are the amount of tax assets that will expire unutilized pursuant to the Section 382 study. This resulted in a reduction of $2.5 million of NOLs and $0.8 million of research and development credits and a corresponding reduction in the valuation allowance of $3.3 million, which was recorded in the 2021 fiscal year. Subsequent ownership changes in future years could trigger additional limitations of our NOLs. During the year ended September 30, 2022, we determined that there were no changes in ownership pursuant to Section 382.

We are subject to healthcare laws and regulations which may require substantial compliance efforts and could expose us to criminal sanctions, civil and administrative penalties, contractual damages, reputational harm and diminished profits and future earnings, among other penalties.

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of our products, if approved. Our arrangements with such persons and third-party payors and our general business operations will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute our drugs, if we obtain marketing approval. Restrictions under applicable U.S. federal, state and foreign healthcare laws and regulations include, but are not limited to, the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, including any kickback, bribe or rebate, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase or lease, order or recommendation of, any item, good, facility or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;

- U.S. federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, which impose criminal and civil penalties, including those from civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government;

- The Stark Law prohibits a physician from making referrals for certain "designated health services" payable by Medicare to an entity in which the physician or an immediate family member of such physician has an ownership or investment interest or with which the physician has entered into a compensation arrangement, unless a statutory exception applies. There are a number of exceptions to the Stark Law. Such exceptions permit certain payments and arrangements that, although they would otherwise potentially implicate the Stark Law, are not treated as a violation under the same if the requirements of the specific exceptions are met.

- HIPAA, which among other things, created additional federal criminal statutes that impose criminal and civil liability for, such actions as executing or attempting to execute a scheme to defraud any healthcare benefit program or knowingly and willingly falsifying, concealing or covering up a material fact or making false statements relating to healthcare matters;

- The privacy and security provisions of HIPAA, which impose certain requirements on covered entities and their business associates, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- U.S. federal transparency requirements under the Physician Payments Sunshine Act, enacted as part of the Affordable Care Act that require applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to track and annually report to CMS payments and other transfers of value provided to physicians, certain other healthcare providers (such as physicians assistants and nurse practitioners),and teaching hospitals, as well as ownership and investment interests held by physicians or their immediate family members; and

- analogous state or foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements, state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA, thus complicating compliance efforts.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices do 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 were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, possible exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could substantially disrupt our operations. If the physicians or other providers or entities with whom we expect to do business are 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. We may incur significant costs achieving and maintaining compliance with applicable federal and state privacy, security, and fraud laws. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our attention from the operation of our business.

We expect current and future legislation affecting the pharmaceutical industry, including drug pricing reform, to impact our business generally, which could adversely affect our business operations.

In the United States, there have been, and continue to be proposed and enacted legislation at the federal and state levels designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. For example, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. If any of our products are subject to such negotiation, we may lose a significant amount of the revenues expected during the full life cycle of these products. Further, the Biden administration released an additional

executive order on October 14, 2022, directing HHS to submit a report within 90 days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

The coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.

Significant uncertainty exists as to the coverage and reimbursement status of any compound for which we may seek regulatory approval. Sales in the United States will depend in part on the availability of sufficient coverage and adequate reimbursement from third-party payors, which include government health programs such as Medicare, Medicaid, CHIP, TRICARE and the Veterans Administration, as well as managed care organizations and private health insurers. Prices at which we or our customers seek reimbursement for our therapeutic compounds can be subject to challenge, reduction or denial by payors.

The process for determining whether a payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be available. Additionally, in the United States there is no uniform policy among payors for coverage or reimbursement. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies, but also have their own methods and approval processes. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. If coverage and adequate reimbursement are not available, or are available only at limited levels, successful commercialization of, and obtaining a satisfactory financial return on, any product we develop may not be possible.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for marketing, we may need to conduct expensive studies in order to demonstrate the medical necessity and cost-effectiveness of any products, which would be in addition to the costs expended to obtain regulatory approvals. Third-party payors may not consider our compounds to be medically necessary or cost-effective compared to other available therapies, or the rebate percentages required to secure favorable coverage may not yield an adequate margin over cost or may not enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development. Additionally, we or our collaborators may develop companion diagnostic tests for use with our product candidates. Companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics. Our inability to promptly obtain coverage and adequate reimbursement from third-party payors for the product candidates, and for us or our collaborators to obtain coverage and adequate reimbursement for related companion diagnostic tests that may be developed, could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to our Common Stock

A decline in the price of our common stock could affect our ability to raise further working capital and adversely impact our operations and would severely dilute existing or future investors if we were to raise funds at lower prices.

A prolonged decline in the price of our common stock could result in a reduction in our ability to raise capital. Because our operations have been financed through the sale of equity securities, a decline in the price of our common stock could be especially detrimental to our continued operations. Any reduction in our ability to raise equity capital in the future would force us to reallocate funds from other planned uses and would have a significant negative effect on our business plans and operations, including our ability to develop new products and continue our current operations. If our stock price declines, there can be no assurance that we can raise additional capital or generate funds from operations sufficient to meet our obligations. We believe the following factors could cause the market price of our common stock to continue to fluctuate widely and could cause our common stock to trade at a price below the price at which you purchase your shares of common stock:

- actual or anticipated variations in our quarterly operating results;
- announcements of new services, products, acquisitions or strategic relationships by us or our competitors;
- changes in accounting treatments or principles;
- changes in earnings estimates by securities analysts and in analyst recommendations; and
- general political, economic, regulatory and market conditions.

The market price for our common stock may also be affected by our ability to meet or exceed expectations of analysts or investors. Any failure to meet these expectations, even if minor, could materially adversely affect the market price of our common stock.

If we issue additional shares of common stock in the future, it will result in the dilution of our existing stockholders and may cause the share price of our common stock to fall.

We have 200,000,000 shares of common stock authorized for issuance and we also have 10,000,000 shares of preferred stock authorized. Our Board of Directors has the authority to issue additional shares of preferred and common stock up to the authorized capital stated in the articles of incorporation. Our Board of Directors may choose to issue some or all such shares of common stock to acquire one or more businesses or to provide additional financing in the future. The issuance of any such shares of common stock will result in a reduction of the book value or market price of the outstanding shares of our common stock. If we do issue any such additional shares of common stock, such issuance also will cause a reduction in the proportionate ownership and voting power of all other stockholders. Further, any such issuance may result in a change of control of our corporation. In the event we do issue or sell additional shares of common or preferred stock, it may result in stockholder dilution and may cause our share price to fall.

Our stock price has been volatile and may be volatile in the future.

Our stock price has been volatile at certain times historically, and may be volatile in the future. We may incur rapid and substantial increases or decreases in our stock price in the foreseeable future that are do not coincide in timing with the disclosure of news or developments by us. The stock market in general, and the market for biotechnology and pharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including the following:

- announcements of new data, clinical trial results or those of companies that are perceived to be similar to us;
- announcements related to any delays in any preclinical or clinical trials related to our products;
- announcements related to our products' ability to demonstrate efficacy or an acceptable safety profile of our product candidates or similar announcements by companies that are perceived to be similar to us;
- our ability to meet or exceed expectations of analysts or investors;
- news that the number of patients required for clinical trials for our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate or the duration of these clinical trials may be longer than we anticipate;
- actions taken by regulatory agencies with respect to our product candidates or the progress of our clinical trials, including with respect to any fast track or orphan drug designations;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic collaboration partners or our competitors;
- grants awarded to us or companies that are perceived to be similar to us from outside entities;
- variations in our financial results or those of companies that are perceived to be similar to us;
- trading volume of our common stock;
- developments concerning our collaborations or partners;
- the impact of the COVID-19 outbreak and its effect on us;
- the perception of the biotechnology or pharmaceutical industries by the public, legislatures, regulators and the investment community;
- developments or disputes concerning intellectual property rights;
- significant lawsuits, including patent or stockholder litigation;
- our ability or inability to raise additional capital and the terms on which we raise it;
- sales of our common stock by us or our stockholders;
- declines in the market prices of stocks generally or of companies that are perceived to be similar to us; and
- general economic, industry and market conditions.

In addition, companies trading in the stock market in general, and The Nasdaq Capital Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects. There can be no guarantee that our stock price will remain at current prices.

Our common stock may become the target of a "short squeeze."

Securities of certain companies have experienced significant and extreme volatility in stock price due to short sellers of shares of common stock, known as a "short squeeze." These short squeezes have caused extreme volatility in those companies and in the market and have led to the price per share of those companies to trade at a significantly inflated rate that is disconnected from the underlying value of the company. Many investors who have purchased shares in those companies at an inflated rate face the risk of losing a significant portion of their original investment as the price per share has declined steadily as interest in those stocks have abated. There can be no assurance that we will not, in the future be, a target of a short squeeze, and you may lose a significant portion or all of your investment if you purchase our shares at a rate that is significantly disconnected from our underlying value.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Pursuant to Section 404 of the Sarbanes-Oxley Act, our management is required to report upon the effectiveness of our internal control over financial reporting. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the Nasdaq Stock Market, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make a required related party transaction disclosure. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Risks Related to our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize product candidates similar or identical to ours, and our ability to successfully commercialize our product candidates that we may pursue may be impaired.

Our success depends in large part on our ability to obtain and maintain protection of our intellectual property, particularly patents, in the United States and other countries with respect to our product candidates and technology. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates or by in-licensing intellectual property. U.S. patents related to ANAVEX®2-73 are directed to a dosage form comprising certain doses of ANAVEX®2-73 and donepezil, and the coverage is limited to the United States only. We may not be able to obtain patent protection for ANAVEX®2-73 as a single drug or in other jurisdictions.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal, technological and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our product candidates, in whole or in part, or which effectively prevent others from commercializing competitive product candidates. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative product candidates in a non-infringing manner.

Moreover, we may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or the USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing on third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical product candidates, or limit the duration of the patent protection of our product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

We hold ownership or exclusive rights to seventeen U.S. patents, nineteen U.S. patent applications, and various PCT or ex-U.S. patent applications relating to our drug candidates, methods associated therewith, and to our research programs. Neither patents nor patent applications ensure the protection of our intellectual property for a number of reasons, including the following:

1. Competitors may interfere with our patenting process in a variety of ways. Competitors may claim that Anavex is not entitled to an issued patent for a variety of legal reasons. Competitors may also claim that we are infringing their patents and restrict our freedom to operate. If a court or, in some circumstances, a board of a national patent authority, agrees, we would lose some or all of our patent protection. As a company, we have no meaningful experience with competitors interfering with our patents or patent applications.
2. Because of the time, money and effort involved in obtaining and enforcing patents, our management may spend less time and resources on developing potential drug compounds than they otherwise would, which could increase our operating expenses and delay product programs.
3. Issuance of a patent may not provide significant practical protection. If we receive a patent of narrow scope, then it may be possible for competitors to design products that do not infringe our patent(s).
4. Anavex is seeking patent protection for a number of indications, combination products and drug regimens. The lack of patent protection in global markets for a specific end product or indication may inhibit our ability to advance our compounds and may make Anavex less attractive to potential partners.
5. Defending a patent lawsuit takes significant time and can be very expensive.
6. If a court decides that an Anavex compound, its method of manufacture or use, infringes on the competitor's patent, we may have to pay substantial damages for infringement.
7. A court may prohibit us from making, selling or licensing the potential drug compound unless the patent holder grants a license. A patent holder is not required to grant a license. If a license is available, we may have to pay substantial royalties or grant cross licenses to our patents, and the license terms may be unacceptable.
8. Redesigning our potential drug compounds so that they do not infringe on other patents may not be possible or could require substantial funds and time.

It is also unclear whether our trade secrets are adequately protected. While we use reasonable efforts to protect our trade secrets, our employees or consultants may unintentionally or willfully disclose our information to competitors. Enforcing a claim that someone illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Our competitors may independently develop equivalent knowledge, methods and know-how.

We may also support and collaborate in research conducted by government organizations, hospitals, universities or other educational institutions. These research partners may be unable or unwilling to grant us exclusive rights to technology or products derived from these collaborations.

If we do not obtain required intellectual property licenses or rights, we could encounter delays in our product development efforts while we attempt to design around other patents or even be prohibited from developing, manufacturing or selling potential drug compounds requiring these rights or licenses. There is also a risk that legal disputes may arise as to the rights to technology or potential drug compounds developed in collaboration with other parties, all with attendant risk, distraction, expense, and lack of predictability.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Depending upon the timing, duration and specifics of FDA marketing approval of product candidates that we identify, one of the U.S. patents covering such product candidate or the use thereof may be eligible for up to five years of patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration sooner, and our revenue could be reduced, possibly materially.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If one of our product candidates is approved and a patent covering that product candidate is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application filed with the FDA to obtain permission to sell a generic version of such product candidate.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

We are party to an exclusive license agreement with Life Science Research Israel Ltd., with respect to certain in-licensed intellectual property related to our ANAVEX®3-71 product candidate, and we may need to obtain additional licenses from others in the future. Our license agreement with Life Science Research Israel Ltd. imposes, and we expect that future license agreements will impose, various development, diligence, commercialization, and other obligations on us. In spite of our efforts, our licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of ANAVEX®3-71 or other product candidates covered by any such future licenses. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our product candidates, technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

If we do not obtain required intellectual property licenses or rights, we could encounter delays in our product development efforts while we attempt to design around other patents or even be prohibited from developing, manufacturing or selling potential drug compounds requiring these rights or licenses. There is also a risk that legal disputes may arise as to the rights to technology or potential drug compounds developed in collaboration with other parties, all with attendant risk, distraction, expense, and lack of predictability.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our success will also depend in part on our ability to commercialize our compounds without infringing the proprietary rights of others. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. We have not conducted extensive freedom of use patent searches and no assurance can be given that patents do not exist or could be issued which would have an adverse effect on our ability to market our technology or maintain our competitive position with respect to our technology. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If our compounds or other subject matter are claimed under other United States patents or other international patents or are otherwise protected by third party proprietary rights, we may be subject to infringement actions. In such event, we may challenge the validity of such patents or other proprietary rights or we may be required to obtain licenses from such companies in order to develop, manufacture or market our technology. There can be no assurances that we would be successful in a challenge or be able to obtain such licenses or that such licenses, if available, could be obtained on commercially reasonable terms. Furthermore, the failure to succeed in a challenge, develop a commercially viable alternative or obtain needed licenses could be materially adverse. Adverse consequences include delays in marketing some or all of our potential drug compounds based on our drug technology or the inability to proceed with the development, manufacture or sale of potential drug compounds requiring such licenses. If we defend ourselves against charges of patent infringement or to protect our proprietary rights against third parties, substantial costs will be incurred regardless of whether we are successful. Such proceedings are typically protracted with no certainty of success. An adverse outcome could subject us to significant liabilities to third parties and force us to curtail or cease the research and development of our technology.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize ANAVEX®2-73 or our other product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Additionally, parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

While we use reasonable efforts to protect our trade secrets, our employees or consultants may unintentionally or willfully disclose our information to competitors. Enforcing a claim that someone illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Our competitors may independently develop equivalent knowledge, methods and know-how.

We seek to protect our confidential proprietary information, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and collaborators. These agreements are designed to protect our proprietary information. However, we cannot be certain that such agreements have been entered into with all relevant parties, and we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. For example, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. We also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. If any of our confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Although we are not currently involved in any litigation, we may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful and could harm our business.

Competitors may infringe our patents or other intellectual property. Although we are not currently involved in any litigation, if we were to initiate legal proceedings against a third party to enforce a patent covering ANAVEX®2-73 or our other product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring ANAVEX®2-73 or our other product candidates to market.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Changes in patent law could diminish the value of our patents and patent applications in general, thereby impairing our ability to protect our product candidates.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications. The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

The risk factors disclosed in this Annual Report on Form 10-K could materially and adversely affect our business, financial condition and results of operations. The risks described herein are not the only risks we face. Our operations could also be affected by additional factors that are not presently known to us or by factors that we currently consider immaterial to our business.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We do not own any real property. We maintain a corporate head office at 630 5th Avenue, 20th Floor, New York, NY, USA. Our lease costs for this office are approximately $9,500 per month. We believe our offices are suitable and adequate to operate our business currently, as they provide us with sufficient space to conduct our operations.

ITEM 3. LEGAL PROCEEDINGS

We know of no material pending legal proceedings, other than ordinary routine litigation incidental to our business, to which our Company or our subsidiary is a party or of which any of their property is subject. There are no proceedings in which any of our directors, officers or affiliates, or any registered or beneficial stockholder holding more than 5% of our shares, is an adverse party or has a material interest adverse to our or our subsidiary's interest.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

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

Market information

Our common stock is quoted on the Nasdaq Global Select Stock Market ("Nasdaq") under the symbol "AVXL."

Holders of Common Stock

As of November 28, 2022, there were approximately 49 stockholders of record, and 77,961,815 shares of our common stock were issued and outstanding. Most of our stockholders hold their shares in street name.

Dividends

We have not paid any cash dividends on our common stock and have no intention of paying any dividends on the shares of our common stock. Our current policy is to retain earnings, if any, for use in our operations and in the development of our business. Our future dividend policy will be determined from time to time by our Board of Directors.

Recent Sales of Unregistered Securities

Since the beginning of our fiscal year ended September 30, 2022, we have not sold any equity securities that were not registered under the Securities Act of 1933 that were not previously reported in a quarterly report on Form 10-Q or in a current report on Form 8-K.

Repurchases of Equity Securities by Our Company and Affiliated Purchasers

None.

ITEM 6 [Reserved]

ITEM 7 MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATION

The following discussion should be read in conjunction with our consolidated financial statements and related notes thereto included elsewhere in this report. Past operating results are not necessarily indicative of results that may occur in future periods. This discussion contains forward-looking statements, which involve a number of risks and uncertainties. See ***Forward Looking Statements*** included elsewhere in this report.

This section discusses year over year comparisons for the fiscal years ended September 30, 2022 and 2021. Discussion of year over year comparisons between the fiscal years ended September 30, 2021 and 2020 have been excluded from this Form 10-K and can be found in "*Management's Discussion and Analysis of Financial Condition and Results of Operations*" in Part II, Item 7 of our Annual Report on Form 10-K for the fiscal year ended September 30, 2021.

Overview

We are in the development stage and have not earned any revenues since our inception in 2004. We do not anticipate earning any revenues until we can establish an alliance with other companies to develop, co-develop, license, acquire or market our products.

Our operating costs consist primarily of research and development activities including the cost of clinical trials and clinical supplies as well as clinical drug manufacturing and formulation. Research and development expenses also include personnel related costs such as salaries and wages, and third-party contract research organization (CRO) expenses in support of these clinical trials. Personnel costs include salaries and wages, benefits, and non-cash stock-based compensation charges associated with options and other equity awards granted to employees and consultants who are directly engaged in support of our research and development activities.

General and administrative expenses consist of personnel costs, expenses for outside professional services and expenses associated with operating as a public company. Personnel costs consist of salaries and wages, benefits and stock-based compensation for general and administrative personnel. Outside professional services and public company expenses, include expenses related to compliance and reporting, additional insurance expenses, audit and SOX compliance, expenses associated with patent research, applications and filings, investor and stockholder relations activities and other administrative expenses and professional services.

Year ended September 30, 2022

During fiscal 2022, we advanced our business and clinical trials through the following events:

- In January 2022, we reported positive top-line results from the placebo-controlled Phase 1 clinical trial (ANAVEX®3-71-001) in development for the treatment of neurodegenerative diseases including Frontotemporal Dementia (FTD), for which ANAVEX®3-71 has been granted Orphan Drug Designation by the FDA. The trial achieved primary and secondary safety endpoints.

- I n February 2022, we reported positive top-line results from the second randomized, placebo-controlled AVATAR Phase 3 clinical trial (ANAVEX®2-73-RS-002) for the treatment of adult patients with Rett syndrome. The trial met its primary and secondary efficacy and safety endpoints, with consistent and clinically meaningful improvements in all efficacy measures.

- In April 2022, we completed the last patient visit in the 48-week open label extension of the Parkinson's Disease Dementia Phase 2 clinical trial.

- In June 2022, the last patient last visit in the randomized, placebo-controlled Phase 2b/3 clinical trial ANAVEX®2-73-AD-004 for the treatment of early Alzheimer's disease occurred. We expect to present top line data at the upcoming Clinical Trial on Alzheimer's Disease (CTAD) Congress 2022 in San Francisco, CA.

- Throughout fiscal 2022, we made significant progress in the randomized, placebo-controlled EXCELLENCE Phase 2/3 clinical trial ANAVEX®2-73-RS-003 for the treatment of pediatric patients with Rett syndrome with expansion of enrollment into clinical sites across Canada and the United Kingdom.

Operating Expenses

Our operating expenses for fiscal 2022 increased to $51.0 million, from $42.0 million in fiscal 2021. The increase is attributable to an increase in research and development expenses of $4.9 million in 2022 to $37.9 million, as described below.

The following table summarizes our research and development expenses for the years ended September 30, 2022, and 2021 (in thousands):

	2022	2021
Costs of external service providers	$ 18,102	$ 21,243
Personnel costs	8,012	6,987
Stock-based compensation	11,250	4,660
License fees	500	—
Other common costs	52	94
Total research and development costs	$ 37,916	$ 32,984

During fiscal 2022, external service providers costs by product candidate were as follows (in thousands):

ANAVEX®2-73	$ 15,510
ANAVEX®3-71	2,251
All other product candidates	298
Other external service provider costs	43
Total external service provider costs	$ 18,102

The decrease in external service provider costs from fiscal 2021 to fiscal 2022 is related to a decrease in clinical trial expenditures over the comparable period, associated with the completion of the enrollment and recruitment activities for our Phase 2b/3 trial in Alzheimer's disease, and manufacturing activities in the comparable period associated with the Rett syndrome program. This decrease was offset by an increase in personnel costs and non-cash stock-based compensation associated with an expanding team directly engaged in support of ongoing research and development activities.

General and administrative expenses for fiscal 2022 increased to $13.1 million, from $9.0 million in fiscal 2021, most significantly related to an increase in personnel and an increase in associated non-cash stock option compensation charges.

During fiscal 2022, we utilized cash and cash equivalents of $24.2 million to fund our operations, compared to $30.4 million during fiscal 2021. Our cash position decreased to $149.2 million at September 30, 2022, a decrease of $2.9 million over the prior year. Cash for operations was generated through the issuance of shares of common stock under the financing arrangements described below.

We will continue to see an increase in our research and development expenditures as we advance our ANAVEX ®2-73 clinical trials, including planned advancement of ANAVEX®2-73 for Parkinson's disease program, planned initiation of a Fragile X clinical program, ongoing extension studies of our current clinical programs, continued advancement of our other pipeline compounds such as ANAVEX®3-71, and as we continue to add additional staffing to manage and support these clinical initiatives.

Other income

Net other income for the year ended September 30, 2022 was $3.4 million as compared to $4.4 million for fiscal 2021. The primary reason for the decrease in other income was due to a decrease in research and development incentive income and an increased foreign exchange loss associated with incentive and other receivables denominated in Australian dollars, and related impact from the fluctuation of the Australian dollar against the US dollar during the year. The decrease was offset by an increase in interest income.

During fiscal 2022, we recorded $3.3 million in research and development incentive income, consisting of the Australian research and development incentive credit administered through the Australian Tax Office, in connection with fiscal 2022 eligible expenditures. In comparison, research and development incentive income for fiscal 2021 was $4.5 million in connection with fiscal 2021 eligible expenditures and fiscal 2020 expenditures for which an overseas finding ruling was obtained during fiscal 2021. We expect to continue to receive support from the Australian government for various clinical trials being conducted within Australia.

Net loss

Net loss for fiscal 2022 was $48.0 million, or $0.62 per share, compared to a net loss of approximately $37.9 million, or $0.54 per share for fiscal 2021.

Liquidity and Capital Resources

Working Capital

	2022	2021
Current Assets	$ 152,704,603	$ 161,616,490
Current Liabilities	10,213,561	10,798,386
Working Capital	$ 142,491,042	$ 150,818,104

At September 30, 2022, we had $149.2 million in cash and cash equivalents, a decrease of $2.9 million, from $152.1 million at September 30, 2021. The decrease in cash and cash equivalents during the year is a result of cash utilized in operations, partially offset by cash provided by financing activities, as described below.

We intend to continue to use our capital resources to advance our clinical trials for ANAVEX ®2-73 and ANAVEX®3-71, and to perform work necessary to prepare for future development of our pipeline compounds.

Cash Flows

	2022	2021
Cash flows used in operating activities	$ (24,237,864)	$ (30,383,674)
Cash flows provided by financing activities	21,287,980	153,242,401
Increase (decrease) in cash	$ (2,949,884)	$ 122,858,727

Cash flow used in operating activities

There was a decrease in cash used in operating activities of $6.1 million during fiscal 2022 primarily due to the collection of incentive and tax receivables.

Cash flow provided by financing activities

Cash provided by financing activities in fiscal 2022 was $21.3 million, net of financing costs, primarily attributable to cash received from the issuance of common shares at various market prices under the Sales Agreement.

Cash provided by financing activities in fiscal 2021 was $153.2 million, net of financing costs, primarily attributable to cash received from the issuance of common shares at various market prices under the 2019 Purchase Agreement, the Sales Agreement and a direct registered offering.

Other Financings

Purchase Agreement

On June 7, 2019, we entered into a Purchase Agreement (the "2019 Purchase Agreement") with Lincoln Park Capital Fund, LLC ("Lincoln Park"), as amended on July 1, 2020, pursuant to which Lincoln Park committed to purchase up to $50.0 million of our common stock. Concurrently with the execution of the 2019 Purchase Agreement in 2019, we issued 324,383 shares of our common stock to Lincoln Park as a fee for its commitment to purchase shares of our common stock under the 2019 Purchase Agreement and became obligated to issue up to 162,191 shares pro rata, when and if Lincoln Park purchased, at our discretion, the $50.0 million aggregate commitment.

During fiscal year 2021, the Company issued to Lincoln Park an aggregate of 4,086,209 shares of common stock under the 2019 Purchase Agreement, including 4,007,996 shares of common stock for an aggregate purchase price of $24.1 million and 78,213 commitment shares. As of September 30, 2022 and 2021, no shares of our common stock remain available for purchase by Lincoln Park under the 2019 Purchase Agreement.

Controlled Equity Offering Sales Agreement

On May 1, 2020, we entered into an Amended and Restated Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co. and SVB Leerink LLC (the "Sales Agents"), pursuant to which we may offer and sell shares of common stock registered under an effective registration statement from time to time through the Sales Agents (the "At-the-Market Offering").

Upon delivery of a placement notice based on our instructions and subject to the terms and conditions of the Sales Agreement, the Sales Agents may sell shares of common stock by methods deemed to be an "at the market offering", in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, or by any other method permitted by law, including negotiated transactions, subject to our prior written consent. We are not obligated to make any sales of shares under the Sales Agreement. We or the Sales Agents may suspend or terminate the At-the-Market Offering upon notice to the other party, subject to certain conditions. The Sales Agents will act as agents on a commercially reasonable efforts basis consistent with their normal trading and sales practices, applicable state and federal law, and rules and regulations and the rules of Nasdaq.

We have agreed to pay the Sales Agents' commissions for their services of 3.0% of the gross proceeds from the sale of shares of common stock pursuant to the Sales Agreement. We have also agreed to provide the Sales Agents with customary indemnification and contribution rights.

During fiscal 2022, 1,623,813 shares were sold pursuant to the At-the-Market Offering for gross proceeds of $21.0 million (net proceeds of $20.3 million after deducting offering expenses).

During fiscal 2021, 5,634,576 shares were sold pursuant to the At-the-Market Offering for gross proceeds of $79.1 million (net proceeds of $76.7 million after deducting commissions and offering expenses).

Registered Direct Offering

On June 24, 2021, the Company completed a registered direct offering off of the Company's shelf registration statement on Form S-3 filed with the SEC on July 3, 2019. The Company issued 2,380,953 common shares at $21.00 per share for gross proceeds of $50.0 million (net proceeds of $46.9 million after deducting offering fees and expenses).

Off-Balance Sheet Arrangements

We have no off-balance sheet arrangements that have or are reasonably likely to have a current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources that are material to our stockholders.

APPLICATION OF CRITICAL ACCOUNTING POLICIES

Our financial statements and accompanying notes are prepared in accordance with generally accepted accounting principles in the United States. Preparing financial statements requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue and expenses. These estimates and assumptions are affected by management's application of accounting policies. We believe that understanding the basis and nature of the estimates and assumptions involved with the following aspects of our financial statements is critical to an understanding of our financial statements.

We base our assumptions and estimates on historical experience and other sources that we believe to be reasonable at the time. Actual results may vary from our estimates due to changes in circumstances, politics, global economics, general business conditions and other factors. Our significant estimates are related to the valuation of warrants and options.

There are accounting policies that we believe are significant to the presentation of our financial statements. The most significant of these accounting policies relates to the accounting for our research and development expenses and stock-based compensation expense.

Research and Development Expenses

Research and development costs are expensed as incurred. These expenses are comprised of the costs of the Company's proprietary research and development efforts, including preclinical studies, clinical trials, manufacturing costs, employee salaries and benefits and stock based compensation expense, contract services including external research and development expenses incurred under arrangements with third parties such as contract research organizations ("CROs"), facilities costs, overhead costs and other related expenses. Milestone payments made by the Company to third parties are expensed when the specific milestone has been achieved. Manufacturing costs are expensed as incurred in accordance with Accounting Standard Codification ("ASC") 730, Research and Development, as these materials have no alternative future use outside of their intended use.

Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and amortized over the period that the goods are delivered, or the related services are performed, subject to an assessment of recoverability. The Company makes estimates of costs incurred in relation to external CROs, and clinical site costs. The Company analyzes the progress of clinical trials, including levels of patient enrollment, invoices received and contracted costs when evaluating the adequacy of the amount expensed and the related prepaid asset and accrued liability. Significant judgments and estimates must be made and used in determining the accrued balance and expense in any accounting period. The Company reviews and accrues CRO expenses and clinical trial study expenses based on work performed and relies upon estimates of those costs applicable to the stage of completion of a study. Accrued CRO costs are subject to revisions as such trials progress to completion. Revisions are charged to expense in the period in which the facts that give rise to the revision become known. With respect to clinical site costs, the financial terms of these agreements are subject to negotiation and vary from contract to contract. Payments under these contracts may be uneven and depend on factors such as the achievement of certain events, the successful recruitment of patients, the completion of portions of the clinical trial or similar conditions. The objective of our policy is to record expenses in our financial statements based on actual services received and efforts expended. As such, expense accruals related to clinical site costs are recognized based on our estimate of the degree of completion of the event or events specified in the specific clinical trial contract.

In addition, we incur expenses in respect of the acquisition of intellectual property relating to patents and trademarks. The probability of success and length of time to develop commercial applications of the drugs subject to the acquired patents and trademarks is difficult to determine and numerous risks and uncertainties exist with respect to the timely completion of the development projects. There is no assurance the acquired patents and trademarks will ever be successfully commercialized. Due to these risks and uncertainties, we expense the acquisition of patents and trademarks.

Stock-based Compensation

We account for all stock-based payments and awards under the fair value-based method.

The fair value of all share purchase options and warrants are expensed over their contractual vesting period, or over the expected performance period for only the portion of awards expected to vest, in the case of milestone-based vesting, with a corresponding increase to additional paid-in capital.

Compensation costs for stock-based payments with graded vesting are recognized on a straight-line basis. Stock based compensation expense is adjusted for actual forfeitures of unvested awards as they occur.

We have granted share purchase option awards that vest upon achievement of certain performance criteria, or milestone-based awards. We estimate an implicit service period for achieving performance criteria for each award and recognizes the resulting fair value as expense over the implicit service period when we conclude that achieving the performance criteria is probable. We periodically review and update as appropriate our estimates of implicit service periods and conclusions on achieving the performance criteria. Performance awards vest upon achievement of the performance criteria.

We use the Black-Scholes option valuation model to calculate the fair value of share purchase options and warrants at the date of the grant. This model requires the input of subjective assumptions, including the expected price volatility, and expected life of each award. These assumptions consist of estimates of future market conditions, which are inherently uncertain, and therefore, are subject to management's judgment. Changes in these assumptions can materially affect the fair value estimates.

RECENT ACCOUNTING PRONOUNCEMENTS

For a discussion of recent accounting pronouncements and their possible effect on our results, see Note 2 to our Consolidated Financial Statements found elsewhere in this Annual Report.

ITEM 7A QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

We invest our excess cash in investment-grade, interest-bearing securities. The primary objective of our investment policy is to preserve principal and liquidity. To achieve this objective, our investment policy allows for investments in domestic money market certificates, certificates of deposit, money market funds, commercial papers, bonds or commercial papers, and establishes diversification and credit quality requirements and limits investments by maturity and issuer. At September 30, 2022 and 2021, the majority of our excess cash was held in a JP Morgan Chase Prime Money Market Fund. The average amount invested at any given time throughout the year ended September 30, 2022 was $132.7 million (high: $133.2 million; low: $132.2 million) and the average rate of return was 0.74%. A hypothetical 100 basis point change in interest rates during any of the periods presented would not have a material impact on the fair market value of our cash and cash equivalents as of September 30, 2022 and 2021. To date, we have not experienced a loss of principal on any of our investments and as of September 30, 2022 we did not have any allowance for credit losses from our cash and cash equivalents.

Foreign Exchange Risk

We face foreign exchange risk as a result of entering into transactions denominated in currencies other than U.S. dollars and as a result of the existence of sales and tax incentive receivables denominated in other than U.S. dollars. Due to the uncertain timing of expected payments in foreign currencies, we do not utilize any forward exchange contracts. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made. Volatile market conditions and supply chain shortages may result in significant changes in exchange rates, and in particular a change in foreign currencies values relative to the U.S. dollar may affect our operating expenses as expressed in U.S. dollars. An adverse movement in foreign exchange rates could have a material effect on payments made to foreign suppliers.

For the year ended September 30, 2022, a majority of our expenses were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates applied to foreign currency transactions for the year ended September 30, 2022 would not have had a material impact on our consolidated financial statements.

At September 30, 2022, we held net assets of $6.4 million (AUD $9.9 million) denominated in Australian dollars. A hypothetical 10% change in foreign exchange rates at September 30, 2022 would result in a change in reported net assets of +/- $0.6 million.

Inflation Risk

Inflation generally may affect us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material impact on our results of operations during the periods presented.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Board of Directors and Shareholders
Anavex Life Sciences Corp.

Opinion on internal control over financial reporting

We have audited the internal control over financial reporting of Anavex Life Sciences Corp. (a Nevada corporation) and subsidiaries (the "Company") as of September 30, 2022, based on criteria established in the 2013 *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of September 30, 2022, based on criteria established in the 2013 *Internal Control—Integrated Framework* issued by COSO.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated financial statements of the Company as of and for the year ended September 30, 2022, and our report dated November 28, 2022 expressed an unqualified opinion on those financial statements.

Basis for opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and limitations of internal control over financial reporting

A company's internal control over financial reporting is a process designed 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. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ GRANT THORNTON LLP

Hartford, Connecticut
November 28, 2022

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Board of Directors and Shareholders
Anavex Life Sciences Corp.

Opinion on the financial statements

We have audited the accompanying consolidated balance sheet of Anavex Life Sciences Corp. (a Nevada corporation) and subsidiaries (the "Company") as of September 30, 2022, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows for the year ended September 30, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of September 30, 2022, and the results of its operations and its cash flows for the year ended September 30, 2022, in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of September 30, 2022, based on criteria established in the 2013 *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"), and our report dated November 28, 2022 expressed an unqualified opinion.

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 audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit 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. Our audit 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 audit 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 audit provides a reasonable basis for our opinion.

Critical audit matters

Critical audit matters are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ GRANT THORNTON LLP

We have served as the Company's auditor since 2022.

Hartford, Connecticut
November 28, 2022

Report of Independent Registered Public Accounting Firm

Shareholders and Board of Directors
Anavex Life Sciences Corp.
New York, New York

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheet of Anavex Life Sciences Corp. (the "Company") as of September 30, 2021, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended September 30, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at September 30, 2021, and the results of its operations and its cash flows for each of the two years in the period ended September 30, 2021**,** in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of September 30, 2021, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") and our report dated November 24, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

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

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ BDO USA, LLP

We served as the Company's auditor from 2013 to 2022.

New York, New York

November 24, 2021

ANAVEX LIFE SCIENCES CORP.
CONSOLIDATED BALANCE SHEETS
As at September 30, 2022 and 2021

	2022	2021
Assets		
Current		
Cash and cash equivalents	**$ 149,157,861**	$ 152,107,745
Incentive and tax receivables	**3,192,580**	9,136,831
Prepaid expenses and other current assets	**354,162**	371,914
Total Assets	**$ 152,704,603**	$ 161,616,490
Liabilities and Stockholders' Equity		
Current Liabilities		
Accounts payable	**$ 3,824,777**	$ 4,739,781
Accrued liabilities (Note 3)	**5,944,953**	5,614,774
Deferred grant income (Note 4)	**443,831**	443,831
Total Liabilities	**10,213,561**	10,798,386
Commitments and Contingencies - Note 6		
Capital stock		
Authorized:		
10,000,000 preferred stock, par value $0.001 per share		
200,000,000 common stock, par value $0.001 per share		
Issued and outstanding:		
77,942,815 common shares (2021 - 75,918,465)	**77,944**	75,920
Additional paid-in capital	**387,976,881**	348,328,048
Accumulated deficit	**(245,563,783)**	(197,585,864)
Total Stockholders' Equity	**142,491,042**	150,818,104
Total Liabilities and Stockholders' Equity	**$ 152,704,603**	$ 161,616,490

See Accompanying Notes to Consolidated Financial Statements

ANAVEX LIFE SCIENCES CORP.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
For the years ended September 30, 2022, 2021 and 2020

	2022	2021	2020
Operating expenses			
General and administrative	**$ 13,070,068**	$ 9,017,511	$ 5,856,609
Research and development	**37,915,747**	32,983,674	25,231,623
Total operating expenses	**50,985,815**	42,001,185	31,088,232
Operating loss	**(50,985,815)**	(42,001,185)	(31,088,232)
Other income (expenses)			
Grant income	**—**	54,100	149,888
Research and development incentive income	**3,323,011**	4,547,099	4,375,025
Interest income, net	**946,988**	26,261	179,973
Foreign exchange (loss) gain, net	**(903,611)**	(267,344)	125,540
Total other income, net	**3,366,388**	4,360,116	4,830,426
Net loss before provision for income taxes	**(47,619,427)**	(37,641,069)	(26,257,806)
Income tax expense, current	**(358,492)**	(267,565)	(22,664)
Net loss and comprehensive loss	**$ (47,977,919)**	$ (37,908,634)	$ (26,280,470)
Net Loss per share			
Basic and diluted	**$ (0.62)**	$ (0.54)	$ (0.45)
Weighted average number of shares outstanding			
Basic and diluted	76,909,993	69,802,960	58,194,894

See Accompanying Notes to Consolidated Financial Statements

ANAVEX LIFE SCIENCES CORP.
CONSOLIDATED STATEMENTS OF CASH FLOWS
For the years ended September 30, 2022 and 2021

	2022	2021	2020
Cash Flows used in Operating Activities			
Net loss	**$ (47,977,919)**	$ (37,908,634)	$ (26,280,470)
Adjustments to reconcile net loss to net cash used in operations:			
Stock-based compensation	**18,379,242**	8,231,403	4,876,906
Changes in working capital balances related to operations:			
Incentive and tax receivables	**5,944,251**	(4,287,491)	(2,206,595)
Prepaid expenses and deposits	**1,387**	88,290	57,159
Accounts payable	**(915,004)**	750,727	465,722
Accrued liabilities	**330,179**	2,298,200	1,800,232
Deferred grant income	**—**	443,831	—
Net cash used in operating activities	**(24,237,864)**	(30,383,674)	(21,287,046)
Cash Flows provided by Financing Activities			
Issuance of common shares	**20,984,667**	153,218,762	28,754,198
Share issue costs	**(706,877)**	(5,550,921)	(403,764)
Proceeds from exercise of warrants	**—**	1,466,500	—
Proceeds from exercise of stock options	**1,010,190**	4,108,060	—
Net cash provided by financing activities	**21,287,980**	153,242,401	28,350,434
Increase (decrease) in cash and cash equivalents during the period	**(2,949,884)**	122,858,727	7,063,388
Cash and cash equivalents, beginning of period	**152,107,745**	29,249,018	22,185,630
Cash and cash equivalents, end of period	**$ 149,157,861**	$ 152,107,745	$ 29,249,018
Supplemental Cash Flow Information			
Cash paid for state and local minimum income taxes	**$ 326,903**	$ 139,531	$ 22,664

See Accompanying Notes to Consolidated Financial Statements

ANAVEX LIFE SCIENCES CORP.
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY
For the years ended September 30, 2022, 2021 and 2020

	Common Stock				
	Shares	Par Value	Additional Paid-in Capital	Accumulated Deficit	Total
Balance, September 30, 2019	52,650,521	$ 52,652	$ 153,633,807	$ (133,396,760)	$ 20,289,699
Shares issued under 2019 purchase agreement					
Purchase shares	7,564,584	7,565	21,246,733	—	21,254,298
Commitment shares	68,943	69	(69)	—	—
Shares issued pursuant to cashless exercise of stock options	721	1	(1)	—	—
Shares issued under Sales Agreement	1,760,429	1,760	7,498,140	—	7,499,900
Less: share issue costs	—	—	(403,764)	—	(403,764)
Share based compensation	—	—	4,876,906	—	4,876,906
Net loss	—	—	—	(26,280,470)	(26,280,470)
Balance, September 30, 2020	62,045,198	62,047	186,851,752	(159,677,230)	27,236,569
Shares issued under 2019 purchase agreement					
Purchase shares	4,007,996	4,008	24,107,190	—	24,111,198
Commitment shares	78,213	78	(78)	—	—
Shares issued pursuant to exercise of stock options	1,421,529	1,421	4,106,639	—	4,108,060
Shares issued under Sales Agreement	5,634,576	5,635	79,101,915	—	79,107,550
Less: share issue costs	—	—	(2,437,523)	—	(2,437,523)
Shares issued pursuant to registered direct offering	2,380,953	2,381	49,997,632	—	50,000,013
Less: share issue costs	—	—	(3,097,032)	—	(3,097,032)
Shares issued pusuant to exercise of warrants	350,000	350	1,466,150	—	1,466,500
Share based compensation	—	—	8,231,403	—	8,231,403
Net loss	—	—	—	(37,908,634)	(37,908,634)
Balance, September 30, 2021	75,918,465	75,920	348,328,048	(197,585,864)	150,818,104
Shares issued pursuant to exercise of stock options	400,537	401	1,009,789	—	1,010,190
Shares issued under Sales Agreement	1,623,813	1,623	20,983,044	—	20,984,667
Less: share issue costs	—	—	(723,242)	—	(723,242)
Share based compensation	—	—	18,379,242	—	18,379,242
Net loss	—	—	—	(47,977,919)	(47,977,919)
Balance, September 30, 2022	77,942,815	$ 77,944	$ 387,976,881	$ (245,563,783)	$ 142,491,042

See Accompanying Notes to Consolidated Financial Statements

Note 1 Business Description and Basis of Presentation

Business

Anavex Life Sciences Corp. ("Anavex" or the "Company") is a clinical stage biopharmaceutical company engaged in the development of differentiated therapeutics by applying precision medicine to central nervous system ("CNS") diseases with high unmet need. Anavex analyzes genomic data from clinical studies to identify biomarkers, which are used to select patients that will receive the therapeutic benefit for the treatment of neurodegenerative and neurodevelopmental diseases. The Company's lead compound ANAVEX®2-73 is being developed to treat Alzheimer's disease, Parkinson's disease and potentially other central nervous system diseases, including rare diseases, such as Rett syndrome, a rare severe neurological monogenic disorder caused by mutations in the X-linked gene, methyl-CpG-binding protein 2 ("MECP2").

Basis of Presentation

These consolidated financial statements have been prepared pursuant to the rules and regulations of the Securities and Exchange Commission ("SEC") and the instructions to Form 10-K and have been prepared under the accounting principles generally accepted in the United States of America ("U.S. GAAP").

Liquidity

All of the Company's potential drug compounds are in the clinical development stage and the Company cannot be certain that its research and development efforts will be successful or, if successful, that its potential drug compounds will ever be approved for sale or generate commercial revenues. To date, we have not generated any revenues from our operations. The Company expects the business to continue to experience negative cash flows for the foreseeable future and cannot predict when, if ever, its business might become profitable.

Management believes that the current working capital position will be sufficient to meet the Company's working capital requirements beyond the next 12 months after the date that these consolidated financial statements are issued. The process of drug development can be costly, and the timing and outcomes of clinical trials is uncertain. The assumptions upon which the Company has based its estimates are routinely evaluated and may be subject to change. The actual amount of the Company's expenditures will vary depending upon a number of factors including but not limited to the design, timing and duration of future clinical trials, the progress of the Company's research and development programs and the level of financial resources available. The Company has the ability to adjust its operating plan spending levels based on the timing of future clinical trials.

Other than our rights related to the Sales Agreement (as defined below in Note 5), there can be no assurance that additional financing will be available to us when needed or, if available, that it can be obtained on commercially reasonable terms. If the Company is not able to obtain the additional financing on a timely basis, if and when it is needed, it will be forced to delay or scale down some or all of its research and development activities.

Coronavirus Disease 2019 (COVID-19)

The recent global outbreak of COVID-19 did not have a material impact on the Company's result of operations or financial condition for the year ended September 30, 2022. However, the future course of the pandemic could have adverse effects in the U.S and global economies and thus negatively impact our business and financial results.

Note 2 Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in accordance with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses in the reporting period. The Company regularly evaluates estimates and assumptions related to accounting for research and development costs, incentive income receivable, valuation and recoverability of deferred tax assets, stock-based compensation and loss contingencies. The Company bases its estimates and assumptions on current facts, historical experience and various other factors that it believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the book values of assets and liabilities and the accrual of costs and expenses that are not readily apparent from other sources. The actual results experienced by the Company may differ materially and adversely from the Company's estimates. To the extent there are material differences between the estimates and the actual results, future results of operations will be affected.

Principles of Consolidation

These consolidated financial statements include the accounts of Anavex Life Sciences Corp. and its wholly owned subsidiaries, Anavex Australia Pty Limited. (“Anavex Australia”), a company incorporated under the laws of Australia, Anavex Germany GmbH, a company incorporated under the laws of Germany, and Anavex Canada Ltd., a company incorporated under the laws of the Province of Ontario, Canada. All inter-company transactions and balances have been eliminated.

Cash and equivalents

The Company considers only those investments which are highly liquid, readily convertible to cash and that mature within three months from the date of purchase to be cash equivalents.

Highly liquid investments that are considered cash equivalents include money market accounts, money market funds and certificates of deposit. The carrying value of cash equivalents approximates fair value due to the short-term maturity of these securities. The Company’s investment policy allows for investments in domestic money market certificates, certificates of deposit, money market funds, bonds or commercial papers, and establishes diversification and credit quality requirements and limits investments by maturity and issuer. The Company currently maintains its investments at one large well known financial institution.

The Company maintains its cash in bank deposit accounts which, at times, may exceed federally insured limits. Accounts are guaranteed by the Federal Deposit Insurance Corporation (FDIC) up to $250,000, under current regulations. At September 30, 2022 and 2021, substantially all of the Company’s cash balances were in excess of these federally insured limits. The Company mitigates this risk by maintaining the majority of its cash balances in a large well-known financial institution. The Company has not experienced any losses in such accounts.

Research and Development Expenses

Research and development costs are expensed as incurred. These expenses are comprised of the costs of the Company’s proprietary research and development efforts, including preclinical studies, clinical trials, manufacturing costs, employee salaries and benefits and stock-based compensation expense, contract services including external research and development expenses incurred under arrangements with third parties such as contract research organizations (“CROs”), facilities costs, overhead costs and other related expenses. Milestone payments made by the Company to third parties are expensed when the specific milestone has been achieved. Manufacturing costs are expensed as incurred in accordance with Accounting Standard Codification (“ASC”) 730, Research and Development, as these materials have no alternative future use outside of their intended use.

Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and amortized over the period that the goods are delivered, or the related services are performed, subject to an assessment of recoverability. The Company makes estimates of costs incurred in relation to external CROs, and clinical site costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies including the phase or completion of events, invoices received and contracted costs. Judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company’s estimates. The Company’s historical accrual estimates have not been materially different from actual costs.

In addition, the Company incurs expenses in respect of intellectual property costs relating to patents and trademarks. The probability of success and length of time to develop commercial applications of the drugs subject to the underlying patent and trademark costs is difficult to determine and numerous risks and uncertainties exist with respect to the timely completion of the development projects. There is no assurance the drugs subject to the underlying patents and trademarks will ever be successfully commercialized.

Due to these risks and uncertainties, the patent and trademark costs do not meet the definition of an asset and thus are expensed as incurred within general and administrative expenses.

Research and Development Incentive Income

The Company is eligible to obtain certain research and development tax credits, including the Australian research and development tax incentive credit (the "Australia R&D credit") through a program administered through the Australian Tax Office (the "ATO") and AusIndustry, a division of the Australian Government's Department of Industry, Innovation and Science ("AusIndustry"), which provides for a cash refund based on a percentage of eligible research and development activities undertaken in Australia by the Company's wholly owned subsidiary, Anavex Australia. Anavex Australia is also eligible under the Australia R&D credit program to receive the cash refund for certain research and development expenses incurred by Anavex Australia outside of Australia, to the extent such expenses are pre-approved by AusIndustry pursuant to an advanced overseas finding application.

The Australia R&D credit program is available to eligible companies with an annual aggregate revenue of less than $20.0 million Australian during the reimbursable period.

The tax incentives are available on the basis of specific criteria with which the Company must comply. Although the tax incentive may be administered through the local tax authority, the Company has accounted for the incentives outside of the scope of ASC Topic 740, Income Taxes ("ASC 740"), since the incentives are not linked to the Company's taxable income and can be realized regardless of whether the Company has generated taxable income in the respective jurisdictions.

With respect to the Australia R&D credit, as there is no authoritative guidance under GAAP for accounting for grants to for-profit business entities, the Company accounts for the grant by analogy to IAS20 *Accounting for Government Grants and Disclosure of Government Assistance* ("IAS 20"). The Company recognizes the Research and Development Incentive income as it incurs costs eligible for reimbursement under the Australia R&D credit Program when it is reasonably assured that the cash incentive will be received, as evidenced through enrollment in the program and when the applicable conditions under the program have been met. The Company accrues for the amount of cash refund it expects to receive in relation to research and development expenses outside of Australia only to the extent it has received advanced approval from AusIndustry, pursuant to an approved advanced overseas finding application.

In addition, Anavex Australia and Anavex Canada incur Goods and Services Tax (GST) on certain services provided by local vendors. As a domestic entity in those jurisdictions, Anavex Australia and Anavex Canada are entitled to a refund of the GST paid. Similarly, Anavex Germany incurs Value Added Tax (VAT) on certain services provided by local vendors, to which it is entitled to a refund of such VAT paid. The Company's estimate of the amount of cash refund it expects to receive related to GST and VAT incurred is included in Incentive and tax receivables in the accompanying consolidated balance sheets.

Basic and Diluted Loss per Share

Basic income/(loss) per common share is computed by dividing net income/(loss) available to common stockholders by the weighted average number of common shares outstanding during the period. Diluted income/(loss) per common share is computed by dividing net income/(loss) available to common stockholders by the sum of (1) the weighted-average number of common shares outstanding during the period, (2) the dilutive effect of the assumed exercise of options and warrants using the treasury stock method and (3) the dilutive effect of other potentially dilutive securities. For purposes of the diluted net loss per share calculation, options and warrants are potentially dilutive securities and are excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive.

As of September 30, 2022, diluted loss per share excludes 13,329,616 potentially dilutive common shares (2021 – diluted loss per share excludes 11,540,903 potentially dilutive common shares; 2020 – diluted loss per share excludes 10,576,266 potentially dilutive common shares) related to outstanding options and warrants, as their effect was anti-dilutive.

Financial Instruments

The book value of the Company's financial instruments, consisting of cash and equivalents, incentive and tax receivables, accounts payable and accrued liabilities approximate their fair value due to the short-term maturity of such instruments. Unless otherwise noted, it is management's opinion that the Company is not exposed to significant interest, currency or credit risks arising from these financial instruments.

Foreign Currency Translation

The functional currency of the Company is the US dollar. Monetary items denominated in a foreign currency are translated into US dollars at exchange rates prevailing at the balance sheet date and non-monetary items are translated at exchange rates prevailing when the assets were acquired, or obligations incurred. Foreign currency denominated expense items are translated at exchange rates prevailing on the transaction date. Unrealized gains or losses arising from the translations are credited or charged to income in the period in which they occur.

The Company has determined that the functional currency of Anavex Australia Pty Limited, Anavex Germany GmbH, and Anavex Canada Ltd. is also the US dollar.

Segment and Geographic Reporting

Operating segments are defined as components of an enterprise for which separate discrete information is available for evaluation by the chief operating decision maker or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business as one operating segment, which is the business of developing novel therapies for the management of CNS diseases.

Grant Income

Grant income is recognized at the fair value of the grant when it is received, and all substantive conditions have been satisfied. Grants received from government and other agencies in advance of the specific research and development costs to which they relate are deferred and recognized in the consolidated statement of operations in the period they are earned and when the related research and development costs are incurred.

Income Taxes

The Company follows the provisions of ASC 740, which requires the asset and liability method of accounting for income taxes. Under the asset and liability method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to temporary differences between the financial statements carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled.

The Company follows the provisions of ASC 740 regarding accounting for uncertainty in income taxes. The Company initially recognizes tax positions in the financial statements when it is more likely than not the position will be sustained upon examination by the tax authorities. Such tax positions are initially and subsequently measured as the largest amount of tax benefit that is greater than 50% likely of being realized upon ultimate settlement with the tax authority assuming full knowledge of the position and all relevant facts. Application requires numerous estimates based on available information. The Company considers many factors when evaluating and estimating its tax positions and tax benefits, and its recognized tax positions and tax benefits may not accurately anticipate actual outcomes. As additional information is obtained, there may be a need to periodically adjust the recognized tax positions and tax benefits. These periodic adjustments may have a material impact on the consolidated statements of operations. At September 30, 2022 the Company did not have any uncertain tax positions.

The Company recognizes interest and penalties related to current income tax expense on the interest income, net line, in the accompanying consolidated statement of operations. Accrued interest and penalties, if any, are included in accrued liabilities on the consolidated balance sheets. There were no interest and penalties related to current income tax expense during the years ended September 30, 2022, 2021 and 2020.

Stock-based Compensation

The Company accounts for all stock-based payments and awards under the fair value method.

The fair value of all share purchase options and warrants are expensed over their contractual vesting period, or over the expected performance period for only the portion of awards expected to vest, in the case of milestone-based vesting, with a corresponding increase to additional paid-in capital.

Compensation costs for stock-based payments with graded vesting are recognized on a straight-line basis. Stock based compensation expense is adjusted for actual forfeitures of unvested awards as they occur.

The Company has granted share purchase option awards that vest upon achievement of certain performance criteria, or milestone-based awards. The Company estimates an implicit service period for achieving performance criteria for each award and recognizes the resulting fair value as expense over the implicit service period when it concludes that achieving the performance criteria is probable. The Company periodically reviews and updates as appropriate its estimates of implicit service periods and conclusions on achieving the performance criteria. Performance awards vest upon achievement of the performance criteria.

The Company uses the Black-Scholes option valuation model to calculate the fair value of share purchase options and warrants at the date of the grant. This model requires the input of subjective assumptions, including the expected price volatility and expected life of each award. The Company uses the U.S. Treasury daily treasury yield curve rates for the expected term of the option as the risk-free rate. The expected term represents the period that options granted are expected to be outstanding using the simplified method. The Company's historical share option exercise experience does not provide a reasonable basis for estimating the expected term. Expected volatility is based on the average of the daily share price changes over the expected term. The Company does not estimate forfeitures and elects to record actual forfeitures as they occur. The Company has not paid any dividends on its common stock historically, therefore no assumption of dividend payments is made in the model. These assumptions consist of estimates of future market conditions, which are inherently uncertain, and therefore, are subject to management's judgment. Changes in these assumptions can materially affect the fair value estimates.

The purchase price of options or warrants may be paid in cash or, if approved by the Company's compensation committee in advance, "net settled" in shares of the Company's common stock. In a net settlement of an option or warrant, the Company does not receive payment of the exercise price from the holder but reduces the number of shares of common stock issued upon the exercise of the stock option or warrant by the smallest number of whole shares that have an aggregate fair market value equal to or over the aggregate exercise price for the option shares covered by the option or warrant exercised. Shares issued pursuant to the exercise of options and warrants are issued from the Company's treasury.

Fair Value Measurements

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants at the measurement date. Assets and liabilities that are measured at fair value are reported using a three-level fair value hierarchy that prioritizes the inputs used to measure fair value. This hierarchy maximizes the use of observable inputs and minimizes the use of unobservable inputs. The three levels of inputs used to measure fair value are as follows:

Level 1 - quoted prices (unadjusted) in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date;

Level 2 - observable inputs other than Level 1, quoted prices for similar assets or liabilities in active markets, quoted prices for identical or similar assets and liabilities in markets that are not active, and model-derived prices whose inputs are observable or whose significant value drivers are observable; and

Level 3 - assets and liabilities whose significant value drivers are unobservable by little or no market activity and that are significant to the fair value of the assets or liabilities.

At September 30, 2022 and 2021, the Company did not have any Level 2 or Level 3 assets or liabilities.

Recently Adopted Accounting Pronouncements

Effective October 1, 2021, the Company adopted Accounting Standards Update (“ASU”) 2019-12, “Simplifying the Accounting for Income Taxes (ASC 740)”, which is intended to simplify various aspects related to accounting for income taxes by removing certain exceptions to the general principles in Topic 740 and clarifying and amending existing guidance to improve consistent application. There was no material impact on the Company’s operations, financial condition, or cash flows.

In November 2021, the Financial Accounting Standards Board (“FASB”) issued ASU 2021-10, “Government Assistance (Topic 832): Disclosures by Business Entities about Government Assistance” (“ASU 2021-10”). ASU 2021-10 increases the transparency of government assistance including the disclosure of (1) the types of assistance, (2) an entity’s accounting for the assistance, and (3) the effect of the assistance on an entity’s financial statements. ASU 2021-10 is effective for fiscal years beginning after December 15, 2021, with early adoption permitted. Upon implementation, the Company may use either a prospective or retrospective method of adoption when adopting the ASU. The adoption of ASU 2021-10 will impact the disclosures related to the research and development incentive income that the Company receives from the ATO for its clinical trials in Australia. The Company currently plans to adopt the provisions of this ASU on October 1, 2022.

Note 3 Accrued Liabilities

The principal components of accrued liabilities consist of:

	2022	2021
Accrued clinical site and patient visits costs	$ 2,031,105	$ 2,035,800
Accrued compensation and benefits	1,297,337	1,201,903
Fixed contract accruals	417,414	649,649
All other accrued liabilities	2,199,097	1,727,422
	$ 5,944,953	$ 5,614,774

Note 4 Other Income

Grant income

During the year ended September 30, 2022, the Company received $ 0 (2021: $497,931; 2020: $0) of a $995,862 research grant awarded during the year ended September 30, 2021, by the Michael J. Fox Foundation for Parkinson's Research. The grant will be used to fund a clinical trial of the Company's lead compound, ANAVEX®2-73 related to Parkinson's disease.

The grant income is being deferred when received and amortized to other income as the related research and development expenditures are incurred. During the year ended September 30, 2022, the Company recognized $Nil (2021: $54,100; 2020: $Nil) of this grant on its statements of operations within grant income. At September 30, 2022 an amount of $443,831 (2021: $443,831) of this grant is recorded as deferred grant income, representing the amount of this grant which has not yet been amortized to other income.

During the year ended September 30, 2017, the Company was awarded grant funding in the amount of $ 597,886. The grant was received in equal quarterly installments over a period of two years ending during the year ended September 30, 2020, in exchange for a commitment to complete clinical testing for a therapeutic drug candidate for the treatment of Rett syndrome.

The grant income was deferred when received and amortized to other income as the related research and development expenditures were incurred. During the year ended September 30, 2020, the Company recognized $149,888 of this grant on its statement of operations as a component of other income. At September 30, 2020, the Company had recognized the full amount of grant funding.

Research and development incentive income

Research and development incentive income represents income earned by the Company's Australian subsidiary, of the Australian research and development tax incentive credit (the "tax incentive credit").

During the year ended September 30, 2022, the Company recorded research and development incentive income of $ 3,323,011 (AUD 4,468,246) (2021: $4,547,099 (AUD 6,068,993); 2020: $4,375,025 (AUD 6,392,266)) in respect of the tax incentive credit for eligible research and development expenses incurred during the year.

The Company evaluates its eligibility under the tax incentive program as of each balance sheet date based on the most current and relevant data available. Although the Company believes that it complies with all the relevant conditions of the program, as a matter of course, the Company may be subject to pre-issue review or audit by the ATO and, the ATO may have different interpretations of certain eligibility requirements. Currently, the Company's tax incentive claims from 2018 to 2022 are open to potential review or audit by the ATO.

Note 5 Equity Offerings

Common Stock

Common shares are voting and are entitled to dividends as declared at the discretion of the Board of Directors.

Preferred Stock

The Company's Board of Directors (the "Board") has the authority to issue preferred stock in one or more series and to fix the rights, preferences, privileges, restrictions and the number of shares constituting any series or the designation of the series.

Registered Direct Offering

On June 22, 2021, the Company and Deep Track Capital entered into a securities purchase agreement pursuant to which the Company sold to Deep Track Capital an aggregate of 2,380,953 shares of common stock at $21 per share in a registered direct offering, for gross proceeds of $50,000,013. Net proceeds of the offering were $46,902,981 after deducting offering fees and expenses.

Sales Agreement

The Company entered into a Controlled Equity Offering Sales Agreement on July 6, 2018, which was amended and restated on May 1, 2020 (the "Sales Agreement") with Cantor Fitzgerald & Co. and SVB Leerink LLC (together the "Sales Agents"), pursuant to which the Company may offer and sell shares of common stock registered under an effective registration statement from time to time through the Sales Agents (the "Offering").

Upon delivery of a placement notice based on the Company's instructions and subject to the terms and conditions of the Sales Agreement, the Sales Agents may sell the Shares by methods deemed to be an "at the market offering" offering, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, or by any other method permitted by law, including negotiated transactions, subject to the prior written consent of the Company. The Company is not obligated to make any sales of Shares under the Sales Agreement. The Company or Sales Agents may suspend or terminate the offering of Shares upon notice to the other party, subject to certain conditions. The Sales Agents will act as agents on a commercially reasonable efforts basis consistent with their normal trading and sales practices and applicable state and federal law, rules and regulations and the rules of Nasdaq.

The Company has agreed to pay the Sales Agents commissions for their services of up to 3.0% of the gross proceeds from the sale of the Shares pursuant to the Sales Agreement. The Company also agreed to provide the Sales Agents with customary indemnification and contribution rights. During the year ended September 30, 2022, 1,623,813 shares were sold pursuant to the Offering for gross proceeds of $ 20,984,667 (net proceeds of $20,261,425 after deducting offering expenses) (2021: 5,634,576 shares were sold for gross proceeds of $ 79,107,550, net proceeds of $76,670,027; 2020: 1,760,429 shares were sold for gross proceeds of $ 7,499,900, net proceeds of $7,096,136). At September 30, 2022, an amount of $ 142,407,882 (2021: $163,392,550) was registered pursuant to an effective registration statement and available to be sold under the Sales Agreement.

2019 Purchase Agreement

On June 7, 2019, the Company entered into a $50,000,000 purchase agreement (the "2019 Purchase Agreement") with Lincoln Park Capital Fund, LLC ("Lincoln Park"), as amended on July 1, 2020, pursuant to which the Company had the right to sell and issue to Lincoln Park, and Lincoln Park was obligated to purchase, up to $50,000,000 in value of its shares of common stock from time to time over a three-year period until July 1, 2022.

In consideration for entering into the 2019 Purchase Agreement, the Company issued to Lincoln Park 324,383 shares of common stock as a commitment fee during the year ended September 30, 2019 and agreed to issue up to 162,191 shares pro rata, when and if, Lincoln Park purchased, at the Company's discretion, the $50,000,000 aggregate commitment.

During the year ended September 30, 2022, the Company did not issue any shares to Lincoln Park under the 2019 Purchase Agreement.

During the year ended September 30, 2021, the Company issued to Lincoln Park an aggregate of 4,086,209 (2020: 7,633,527) shares of common stock under the 2019 Purchase Agreement, including 4,007,996 (2020: 7,564,584) shares of common stock for an aggregate purchase price of $ 24,111,198 (2020: $21,254,298) and 78,213 (2020: 68,943) commitment shares.

At September 30, 2022 and 2021, no shares remained available for issuance under the 2019 Purchase Agreement.

Note 6 Commitments and Contingencies

Lease

During the year ended September 30, 2022, the Company incurred office lease expense of $ 72,865 (2021: $130,784; 2020: $233,423).

Employee 401(k) Benefit Plan

The Company has a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code. The plan covers all United States based employees. United States based employees eligible to participate in the plan may contribute up to the current statutory limits under the Internal Revenue Service regulations. The 401(k) plan permits the Company to make additional matching contributions on behalf of contributing employees. During the year ended September 30, 2022, the Company made $158,112 (2021: $128,856; 2020: $98,058) in matching contributions under the 401(k) plan.

Litigation

The Company is subject to claims and legal proceedings that arise in the ordinary course of business. Such matters are inherently uncertain, and there can be no guarantee that the outcome of any such matter will be decided favorably to the Company or that the resolution of any such matter will not have a material adverse effect upon the Company's consolidated financial statements. The Company does not believe that any of such pending claims and legal proceedings will have a material adverse effect on its consolidated financial statements.

Share Purchase Warrants

The following table summarizes the warrant activity during the years ended September 30, 2022:

	Number of Shares	Weighted Average Exercise Price ($)
Balance, September 30, 2021	210,000	5.69
Forfeited	(50,000)	12.00
Balance, September 30, 2022	160,000	3.72

On September 30, 2022, the Company had share purchase warrants outstanding as follows:

Number	Exercise Price	Expiry Date
150,000	$ 3.17	May 6, 2024
10,000	$ 12.00	April 21, 2026
160,000		

Stock–based Compensation Plan

2015 Stock Option Plan

On September 18, 2015, the Company's board of directors approved a 2015 Omnibus Incentive Plan (the "2015 Plan"), which provided for the grant of stock options and restricted stock awards to directors, officers, employees and consultants of the Company.

The maximum number of our common shares reserved for issue under the plan was 6,050,553 shares, subject to adjustment in the event of a change of the Company's capitalization.

2019 Stock Option Plan

On January 15, 2019, the Board approved the 2019 Omnibus Incentive Plan (the "2019 Plan"), which provides for the grant of stock options and restricted stock awards to directors, officers, employees, consultants and advisors of the Company.

The maximum number of our common shares reserved for issue under the plan was 6,000,000 shares, subject to adjustment in the event of a change of the Company's capitalization.

During the year ended September 30, 2022, 406,453 options previously available under the 2019 Plan and the 2015 Plan became available under the 2022 Plan (as defined below).

2022 Stock Option Plan

On March 25, 2022, the Board approved the 2022 Omnibus Incentive Plan (the "2022 Plan"). The 2022 Plan was approved by stockholders on May 24, 2022. Under the terms of the 2022 Plan, 10,000,000 additional shares of Common Stock will be available for issuance under the 2022 Plan. Any awards outstanding under a previous stock option plan will remain subject to and be paid under such plan, and any shares subject to outstanding awards under a previous plan that subsequently cease to be subject to such awards (other than by reason of settlement of the awards in shares) will automatically become available for issuance under the 2022 Plan.

The 2022 Plan provides that it may be administered by the Board, or the Board may delegate such responsibility to a committee. The exercise price will be determined by the Board at the time of grant shall be at least equal to the fair market value on such date. If the grantee is a 10% stockholder on the grant date, then the exercise price shall not be less than 110% of fair market value of the Company's shares of common stock on the grant date. Stock options may be granted under the 2022 Plan for an exercise period of up to ten years from the date of grant of the option or such lesser periods as may be determined by the Board, subject to earlier termination in accordance with the terms of the 2022 Plan. At September 30, 2022, 2,058,000 options had been issued under the 2022 Plan and 8,363,453 options were available for issue under the 2022 Plan.

The following summarizes information about stock option activity during the year ended September 30, 2022:

	Number of Shares	Weighted Average Exercise Price ($)	Weighted Average Grant Date Fair Value ($)	Aggregate intrinsic value ($)
Outstanding, September 30, 2021	11,330,903	5.74		140,132,451
Granted	2,358,000	10.13	7.07	—
Forfeited	(118,750)	6.86	5.23	—
Exercised	(400,537)	2.52	1.88	4,201,015
Outstanding, September 30, 2022	13,169,616	6.61		62,267,309
Exercisable, September 30, 2022	8,777,113	4.40		55,173,997

The following summarizes information about stock options at September 30, 2022 by a range of exercise prices:

Range of exercise prices From	To	Number of outstanding options	Weighted average remaining contractual life (in years)	Weighted average exercise price ($)	Number of vested options	Weighted average exercise price ($)
$ 0.92	$ 2.96	3,903,762	5.12	2.30	3,883,345	2.30
$ 3.15	$ 4.80	2,078,800	5.34	3.30	2,063,800	3.29
$ 5.04	$ 8.98	3,957,054	6.07	6.28	2,365,387	6.31
$ 9.20	$ 13.01	1,698,000	9.58	10.50	109,581	12.40
$ 13.22	$ 24.58	1,532,000	8.44	18.23	355,000	18.66
		13,169,616			8,777,113	

The weighted average per share fair value of options vested during the year ended September 30, 2022 was $ 4.69 (2021: $2.54, 2020: $2.55). At September 30, 2022, the weighted average contractual life of options outstanding was 6.4 years (2021: 6.8 years) and for options exercisable was 5.1 years (2021: 5.5 years).

The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying awards and the quoted market price of the Company's stock for the options that were in-the-money at September 30, 2022.

The Company recognized stock-based compensation expense of $18,379,242 during the year ended September 30, 2022 (2021: $ 8,231,403; 2020: $4,876,906) in connection with the issuance and vesting of stock options and warrants in exchange for services. These amounts have been included in general and administrative expenses and research and development expenses on the Company's consolidated statements of operations as follows:

	2022	2021	2020
General and administrative	$ 7,129,412	$ 3,571,335	$ 2,210,789
Research and development	11,249,830	4,660,068	2,666,117
Total stock-based compensation	$ 18,379,242	$ 8,231,403	$ 4,876,906

An amount of approximately $19,032,000 in stock-based compensation is expected to be recorded over the remaining term of such options and warrants through fiscal 2025.

The fair value of each option and warrant award is estimated on the date of grant using the Black Scholes option pricing model based on the following weighted average assumptions:

	2022	2021	2020
Risk-free interest rate	3.11%	0.73%	1.57%
Expected life of options (years)	5.57	5.74	5.53
Annualized volatility	84.17%	93.43%	95.99%
Dividend rate	0.00%	0.00%	0.00%

The fair value of stock compensation charges recognized during the years ended September 30, 2022, 2021 and 2020 was determined with reference to the quoted market price of the Company's shares on the grant date.

Note 7 Income Taxes

The Company's U.S. and foreign loss before income taxes are set forth below:

	2022	2021	2020
United States	$ (40,001,893)	$ (28,850,926)	$ (18,096,148)
Foreign	(7,617,534)	(8,790,143)	(8,161,658)
Total	$ (47,619,427)	$ (37,641,069)	$ (26,257,806)

The components of net deferred income tax assets as of September 30, 2022 and 2021 are as follows:

	2022	2021
Net operating loss carryforwards	$ 46,208,000	$ 34,982,000
Research and development tax credit carryforwards	2,182,000	1,577,000
Stock-based compensation	13,373,000	10,453,000
Unpaid charges	894,000	89,000
Intangible asset costs	388,000	323,000
Foreign exchange and other	44,000	62,000
Valuation allowance of deferred tax assets	(63,089,000)	(47,486,000)
Net deferred tax assets	$ —	$ —

A reconciliation of income tax expense at the statutory federal income tax rate and income taxes as reflected in the consolidated financial statements for the years ended September 30, 2022 and 2021 is as follows:

	2022	2021	2020
Income tax benefit at statutory federal rate	$ (10,000,000)	$ (7,934,000)	$ (5,519,000)
Foreign income taxed at other rates	(170,000)	(353,000)	(723,000)
Permanent differences relating to stock based compensation	(714,000)	(4,379,000)	—
Permanent differences relating to Section 162(m)	—	816,000	—
Other permanent differences	—	741,000	35,000
Adjustment to tax assets based on Section 382	—	3,330,000	—
Research and development credits, net	232,000	1,042,000	1,267,000
State and local taxes	(4,975,000)	(7,022,000)	(2,911,000)
Adjustment to true up to prior years' tax provision	24,000	48,000	373,000
Effect of change in statutory tax rates	—	216,000	36,000
State minimum and excise taxes	358,492	267,565	22,664
Change in valuation allowances	15,603,000	13,495,000	7,442,000
Income tax expense	$ 358,492	$ 267,565	$ 22,664

As of September 30, 2022, the Company had U.S. federal net operating loss carryforwards of approximately $ 123.4 million (2021: $101.6 million) of which $37.7 million will begin to expire in 2025 and $85.7 million can be carried forward indefinitely , state and local net operating loss carryforwards of approximately $199.0 million (2021: $177.7 million) which will begin to expire in 2036, and Research and Development tax credits of $ 2.2 million (2021: $1.6 million) which will begin to expire in 2029. The Company had approximately $ 10.6 million (approximately AU$ 14.9 million) (2021: $7.9 million (approximately AU$ 11.2 million)) of net operating loss carryforwards in Australia, which have an indefinite life, available to offset future taxable income in those jurisdictions.

The Company evaluates its valuation allowance requirements based on available evidence. When circumstances change, and this causes a change in management's judgment about the recoverability of deferred tax assets, the impact of the change on the valuation allowance is reflected in current income. Because management of the Company does not currently believe that it is more likely than not that the Company will receive the benefit of these assets, a full valuation allowance has been established at September 30, 2022 and 2021.

The Company files income tax returns in the U.S. federal jurisdiction and various state and local and foreign jurisdictions. The Company's tax returns are subject to tax examinations by U.S. federal and state tax authorities, or examinations by foreign tax authorities until the respective statutes of limitation expire. The Company is subject to tax examinations by tax authorities for all taxation years commencing on or after 2018.

Under the provisions of the Internal Revenue Code, the net operating loss ("NOL") carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Under Section 382 of the Internal Revenue Code, NOL and tax credit carryforwards may become subject to an annual limitation in the event of an over 50% cumulative change in the ownership interest of significant stockholders over a three-year period, as well as similar state tax provisions.

The Company conducted a Section 382 study during the year ended September 30, 2021 and determined that, during the year ended September 30, 2015, there was a change in ownership which resulted in $25.8 million of federal NOLs being subject to an annual limitation of $439,914. During the year ended September 30, 2021, the Company reduced its federal NOLs by $12.1 million and its Research and Development tax credit carryforwards by $0.8 million, which are the amount of tax assets that will expire unutilized pursuant to the Section 382 study. This resulted in a reduction of $2.5 million of NOLs and $0.8 million of research and development credits and a corresponding reduction in the valuation allowance of $3.3 million, which was recorded in the 2021 fiscal year. Subsequent ownership changes in future years could trigger additional limitations of the Company's NOLs. During the year ended September 30, 2022 the Company determined that there were no changes in ownership pursuant to Section 382.

As of September 30, 2022, the Company did not provide any foreign withholding taxes related to its foreign subsidiaries' undistributed earnings, as such earnings have been retained and are intended to be indefinitely reinvested to fund ongoing operations of the foreign subsidiaries. It is not practicable to estimate the amount of taxes that would be payable upon remittance of these earnings, because such tax, if any, is dependent upon circumstances existing if and when remittance occur.

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

Not Applicable

ITEM 9A. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to provide reasonable assurance that material information required to be disclosed in our periodic reports filed under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and to provide reasonable assurance that such information is accumulated and communicated to our management, our chief executive officer and our principal financial officer, to allow timely decisions regarding required disclosure.

We carried out an evaluation, under the supervision and with the participation of our management, including our principal executive and principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rule 13(a)-15(e) under the Exchange Act. Based on this evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of September 30, 2022.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Under the supervision and with the participation of our management, including our Principal Executive Officer and Principal Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on criteria established in the framework in Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO").

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risks that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Based on this evaluation, our management concluded that our internal controls over financial reporting were effective as of September 30, 2022.

The effectiveness of our internal control over financial reporting as of September 30, 2022, has been audited by Grant Thornton LLP, an independent registered public accounting firm, as stated in their report which appears in this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

During the quarter ended September 30, 2022, there were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a 15(d) or 15d 15(d) of the Exchange Act that materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

ITEM 9B OTHER INFORMATION

None.

PART III

ITEM 10 DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item will be set forth in the section headed "—Election of Directors" and "Information Regarding the Board of Directors and Corporate Governance" in our definitive Proxy Statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after our year ended September 30, 2022 (our "Proxy Statement") and is incorporated in this report by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item will be set forth in the section headed "Executive Compensation" in our Proxy Statement and is incorporated in this report by reference.

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

The information required by this Item will be set forth in the section headed "Security Ownership of Certain Beneficial Owners and Management " in our Proxy Statement and is incorporated in this report by reference.

Information regarding our equity compensation plans will be set forth in the section headed "Executive Compensation" in our Proxy Statement and is incorporated in this report by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item will be set forth in the section headed "Transactions With Related Persons" in our Proxy Statement and is incorporated in this report by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item will be set forth in the section headed "—Ratification of Selection of Independent Registered Public Accounting Firm" in our Proxy Statement and is incorporated in this report by reference.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

Exhibit Number	Description
(3)	**Articles of Incorporation and Bylaws**
3.1	Articles of Incorporation, as amended (incorporated by reference to our Annual Report on Form 10-K filed on November 24, 2021)
3.3	Bylaws (incorporated by reference to our Current Report on Form 8-K filed on September 28, 2007)
(4)	**Instruments Defining the Rights of Security Holders**
4.1	Description of Registrant's Securities*
(10)	**Material Contracts**
10.1^	2015 Omnibus Incentive Plan (incorporated by reference to our Annual Report on Form 10-K filed on December 29, 2015)
10.2^	2019 Omnibus Incentive Plan (incorporated by reference to our Proxy Statement, dated February 11, 2019, as filed on February 11, 2019)
10.3^	2022 Omnibus Incentive Plan (incorporated by reference to our Registration Statement on Form S-8, as filed on June 10, 2022)
10.4^	Employment Agreement, dated as of July 5, 2013, by and between the Company and Christopher Missling, PhD (incorporated by reference to our Quarterly Report on Form 10-Q filed on August 13, 2014)
10.5^	First Amendment to Employment Agreement, dated as of July 5, 2016, by and between the Company and Christopher Missling, PhD (incorporated by reference to our Current Reporton Form 8-K filed on July 7, 2016)
10.6^	Amended and Restated First Amendment to Employment Agreement, dated as of July 18, 2016, by and between the Company and Christopher Missling, PhD (incorporated by reference to our Current Report on Form 8-K filed on July 22, 2016)
10.7^	Second Amendment to Employment Agreement, dated as of May 3, 2019 by and between the Company and Christopher Missling, PhD (incorporated by reference to our Quarterly Report on Form 10-Q filed on May 9, 2019)
10.8^	Third Amendment to Employment Agreement, dated April 7, 2022 by and between the Company and Christopher Missling, PhD (incorporated by reference to our Current Report on Form 8-K filed on April 8, 2022)
10.9^	Amended and Restated Employment Agreement by and between the Company and withSandra Boenisch (incorporated by reference to our Annual Report on Form 10-K filed on December 11, 2017)
10.10^	Amendment No. 1 to Amended and Restated Employment Agreement between the Company and Sandra Boenisch, dated February 4, 2020 (incorporated by reference to our Quarterly Report on Form 10-Q filed on February 6, 2020)
10.11^	Amendment No. 2 to Amended and Restated Employment Agreement between the Company and Sandra Boenisch, dated February 28, 2022 (incorporated by reference to our Current Report on Form 8-K filed on March 4, 2022)
10.12	Amended and Restated Sales Agreement, dated May 1, 2020, by and among the Company, Cantor Fitzgerald & Co. and SVB Leerink LLC (incorporated by reference to our Current Report on Form 8-K filed on May 1, 2020)

Exhibit Number	Description
(14)	**Code of Ethics**
14.1	Code of Ethics Adopted on September 13, 2016 (incorporated by reference to our Annual Report on Form 10-K filed on December 14, 2016)
(21)	**Subsidiaries**
21.1*	Subsidiaries of the Registrant
(23)	**Consent**
23.1*	Consent of Grant Thornton LLP Independent Registered Public Accounting Firm
23.2*	Consent of BDO USA LLP Independent Registered Public Accounting Firm
(31)	**Section 302 Certifications**
31.1*	Section 302 Certification of Christopher Missling, PhD.
31.2*	Section 302 Certification of Sandra Boenisch
(32)	**Section 906 Certifications**
32.1*	Section 906 Certification of Christopher Missling, PhD and Sandra Boenisch
(101)	**XBRL**
101.INS*	XBRL INSTANCE DOCUMENT
101.SCH*	XBRL TAXONOMY EXTENSION SCHEMA
101.CAL*	XBRL TAXONOMY EXTENSION CALCULATION LINKBASE
101.DEF*	XBRL TAXONOMY EXTENSION DEFINITION LINKBASE
101.LAB*	XBRL TAXONOMY EXTENSION LABEL LINKBASE
101.PRE*	XBRL TAXONOMY EXTENSION PRESENTATION LINKBASE
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* Filed herewith.

^ Denotes a management contract or compensatory plan or arrangement.

ITEM 16. FORM 10-K SUMMARY

Not Applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: November 28, 2022

ANAVEX LIFE SCIENCES CORP.

By: */s/ Christopher Missling, PhD*
Name: Christopher Missling, PhD
Title: Chief Executive Officer (Principal Executive Officer)

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.

Signatures	Title(s)	Date
/s/ Christopher Missling, PhD Christopher Missling, PhD	Chief Executive Officer (Principal Executive Officer)	November 28, 2022
/s/ Sandra Boenisch Sandra Boenisch, CPA, CGA	Principal Financial Officer and Treasurer (Principal Accounting Officer)	November 28, 2022
/s/ Athanasios Skarpelos Athanasios Skarpelos	Director	November 28, 2022
/s/ Claus van der Velden, PhD Claus van der Velden, PhD	Director	November 28, 2022
/s/ Steffen Thomas, PhD Steffen Thomas, PhD	Director	November 28, 2022
/s/ Peter Donhauser, D.O. Peter Donhauser, D.O.	Director	November 28, 2022
/s/ Jiong Ma, PhD Jiong Ma, PhD	Director	November 28, 2022