



# 2024 Annual Report

**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, 2024**

☐ 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 ☐

Non-accelerated filer ☒

Accelerated filer ☐

Smaller reporting company ☒

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 ☒

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the 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: \$412 million based on a price of \$5.09 per share, being the closing price of the registrant’s common stock on March 31, 2024.

Indicate the number of shares outstanding of each of the registrant’s classes of common stock, as of the latest practicable date: 84,815,517 issued and outstanding as of December 23, 2024.

#### 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;
- 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 product 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 studies 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 focus is on developing innovative treatments for Alzheimer’s disease, Parkinson’s disease, schizophrenia, neurodevelopmental, neurodegenerative, and rare diseases, including Rett syndrome, and other central nervous system (CNS) disorders.

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:

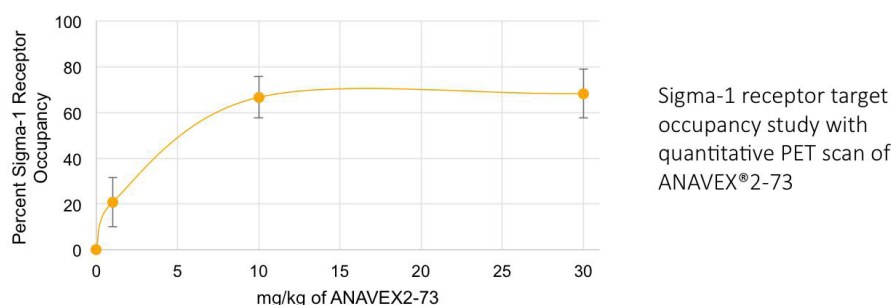
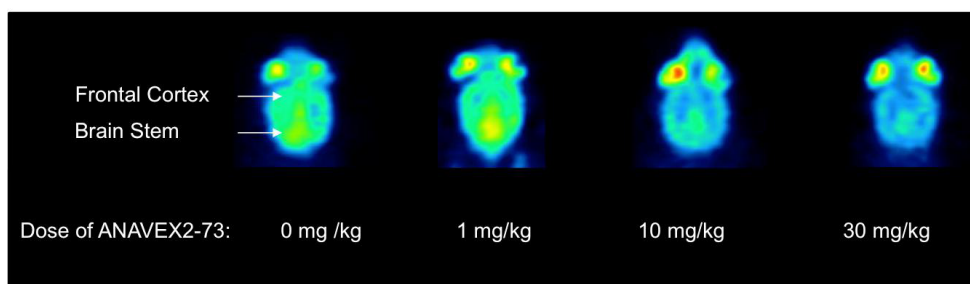
CANDIDATE	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PHASE OLE
<b>ANAVEX®2-73</b> <b>blarcamesine</b> 	ALZHEIMER'S DISEASE		AD ANAVEX®2-73-AD-004		AD ANAVEX®2-73-AD-004 OLE
	PARKINSON'S DISEASE DEMENTIA		ANAVEX®2-73-PDD-001		
	PARKINSON'S DISEASE		ANAVEX®2-73-PET-001	ANAVEX®2-73-PD-001	
	*RETT SYNDROME		EXCELLENCE ANAVEX®2-73-RS-003		ANAVEX®2-73-RS-003 OLE / COMPASSIONATE USE
	*RETT SYNDROME		AVATAR ANAVEX®2-73-RS-002		ANAVEX®2-73-RS-002 OLE / COMPASSIONATE USE
	*RETT SYNDROME		ANAVEX®2-73-RS-001		Fast Track, Rare Pediatric, Orphan Drug (U.S./EU)
	UNDISCLOSED RARE DISEASE				
	*FRAGILE X				
	ANGELMAN'S				
	*INFANTILE SPASMS				
<b>ANAVEX®3-71</b> <b>AF710B</b>	SCHIZOPHRENIA	ANAVEX®3-71-001	ANAVEX®3-71-SZ-001		
	*FRONTOTEMPORAL DEMENTIA (FTD)	ANAVEX®3-71-001			
	ALZHEIMER'S DISEASE	ANAVEX®3-71-001			
<b>ANAVEX®1-41</b>	DEPRESSION				
	STROKE				
	NEURODEGENERATIVE DISEASES				
<b>ANAVEX®1066</b>	VISCERAL PAIN				
	ACUTE & NEUROPATHIC PAIN				

Legend
Solid color = completed
Gradient color = ongoing
Dashed lines = planned
OLE = Open Label Extension

\* = Orphan Drug Designation by the FDA

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 (blarcamesine) target engagement or receptor occupancy with SIGMAR1 in the brain.

## 2D [<sup>18</sup>F]FTC-146-PET imaging of ANAVEX®2-73



Reyes S et al, AAIC 2018

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, 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 (blarcamesine), 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 (blarcamesine)-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 (blarcamesine) has helped us identify actionable genetic variants. A significant impact of the genomic biomarkers SIGMAR1, the direct target of ANAVEX®2-73 (blarcamesine) and COMT, a gene involved in memory function, on the drug response level was identified, leading to an early ANAVEX®2-73 (blarcamesine) 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 (blarcamesine), 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 (blarcamesine) by using genetic biomarkers identified within the trial population itself to either confirm the mechanism of action of ANAVEX®2-73 (blarcamesine) or target patients who are most likely to respond to ANAVEX®2-73 (blarcamesine) treatment. We may in the future utilize such an approach in Alzheimer's disease as well as indications like Parkinson's disease dementia in which ANAVEX®2-73 (blarcamesine) 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<sup>®</sup>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<sup>®</sup>2-73 in 32 patients. ANAVEX<sup>®</sup>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<sup>®</sup>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<sup>®</sup>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<sup>®</sup>2-73, providing 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<sup>®</sup>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<sup>®</sup>2-73 in early Alzheimer's disease commenced in August 2018. The Phase 2b/3 trial enrolled 508 patients, which were treated with a convenient once-daily oral formulation of ANAVEX<sup>®</sup>2-73 for 48 weeks, randomized 1:1:1 to two different ANAVEX<sup>®</sup>2-73 doses or placebo. The trial took place at 52 sites across North America, Europe and Australia. Primary and secondary endpoints to assess safety and both cognitive and functional efficacy, were measured through the Alzheimer's Disease Assessment Scale – Cognitive Subscale test ("ADAS-Cog"), Alzheimer's Disease Cooperative Study – Activities of Daily Living ("ADCS-ADL") and Clinical Dementia Rating – Sum of Boxes for cognition and function ("CDR-SB"). In addition to these endpoints, the ANAVEX<sup>®</sup>2-73 Phase 2b/3 trial design incorporated pre-specified statistical analyses related to potential genomic precision medicine biomarkers previously identified in the ANAVEX<sup>®</sup>2-73 Phase 2a clinical trial. The trial was completed in mid-2022 and, in December 2022, the Company presented topline results from the Phase 2b/3 clinical trial. All statistical analyses were performed by outside consultancy companies.

Furthermore, all pre-specified clinical endpoints were analyzed using a mixed model for repeated measures (MMRM). Under the multiplicity control rule, a trial is successful in meeting the co-primary endpoints if the significance of each endpoint is  $P < 0.05$ , or if the significance of only one co-primary endpoint is  $P < 0.025$ . If only one primary endpoint is significant at an  $\alpha$  level of 0.025, then the secondary endpoint will be evaluated at the same level of 0.025. The trial was successful, the differences in the least-squares mean (LSM) change from baseline to 48 weeks between the ANAVEX<sup>®</sup>2-73 and placebo groups for ADAS-Cog13 was significant at a level of  $P < 0.025$  and for CDR-SB was significant at a level of  $P < 0.025$ , in the patients with early Alzheimer's disease.

The comparison of individual dose groups vs placebo also supports blarcamesine's efficacy. For the primary endpoint ADAS-Cog13, blarcamesine is significantly better than placebo ( $-2.027$ ;  $P = 0.0079$ ) as well as for both the 50 mg ( $-2.149$ ;  $P = 0.021$ ) and the 30 mg ( $-1.934$ ;  $P = 0.026$ ) blarcamesine dosage groups at Week 48, representing that blarcamesine slowed clinical progression at 48 weeks by 36.3% and by 38.5% and 34.6% in 50 mg and 30 mg groups vs. placebo, respectively. The functional co-primary endpoint, ADCS-ADL, was trending in a positive direction but did not reach significance at Week 48. The key secondary endpoint CDR-SB was significantly improved vs. placebo ( $-0.483$ ,  $P = 0.0104$ ) as well as in both 50 mg ( $-0.465$ ;  $P = 0.045$ ) and 30 mg ( $-0.502$ ;  $P = 0.020$ ) groups at Week 48. Clinical Global Impression – Improvement ("CGI-I") was also significantly improved vs. placebo ( $-0.278$ ,  $P = 0.004$ ) as well as in both the 50 mg ( $-0.314$ ;  $P = 0.008$ ) and the 30 mg ( $-0.248$ ;  $P = 0.024$ ) groups at Week 48. The findings are supported by biomarkers, including plasma A $\beta$ 42/40-ratio and reduction of brain atrophy. Blarcamesine significantly slowed brain atrophy in key regions of interest, including the whole brain by 37.6%, total grey matter by 63.5%, and lateral ventricles by 25.1%.

In the respective safety population, common treatment-emergent adverse events included dizziness, which was transient and mostly mild to moderate in severity, and occurred in 120 participants (35.8%) during titration and in 76 participants (25.2%) during maintenance with ANAVEX<sup>®</sup>2-73 and 10 (6.0%) during titration and 9 (5.6%) during maintenance with placebo.

In November 2024, we announced the submission of a Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) for ANAVEX<sup>®</sup>2-73 for the treatment of Alzheimer's disease and, in December 2024, the EMA accepted the

submission for scientific review. The MAA, if approved, would allow direct market access throughout the European Union for oral ANAVEX<sup>®</sup>2-73 (blarcamesine) for the treatment of Alzheimer's disease.

A subsequent long-term open label extension study of ANAVEX<sup>®</sup>2-73, referred to as the ATTENTION-AD trial, was initiated for patients who completed the 48-week Phase 2b/3 placebo-controlled trial referenced above. This trial extension for a duration of up to 96/144 additional weeks was completed in June 2024. The trial extension will provide additional longer-term safety and efficacy data of ANAVEX<sup>®</sup>2-73 in persons with early Alzheimer's disease.

### *Rett Syndrome*

In February 2016, we presented positive preclinical data for ANAVEX<sup>®</sup>2-73 in Rett syndrome, a rare neurodevelopmental disease. The data demonstrated dose related significant improvements in an array of behavioral and gait paradigms in a mouse model with an 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<sup>®</sup>2-73 for the treatment of Rett syndrome.

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

The first Phase 2 trial, (ANAVEX<sup>®</sup>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<sup>®</sup>2-73 formulation in 25 adult female patients with Rett syndrome over a 7-week treatment period including ANAVEX<sup>®</sup>2-73-specific genomic precision medicine biomarkers. The primary endpoint of the trial was safety. The dosing of 5 mg ANAVEX<sup>®</sup>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<sup>®</sup>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<sup>®</sup>2-73 treatment resulted in a sustained improvement in 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<sup>®</sup>2-73 clinical trials, patients carrying the common form of the SIGMAR1 gene treated with ANAVEX<sup>®</sup>2-73 experienced stronger improvements in the prespecified efficacy endpoints. No other clinical trials with ANAVEX<sup>®</sup>2-73 related to Rett syndrome have been conducted in the United States.

The second, international trial of ANAVEX<sup>®</sup>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<sup>®</sup>2-73 in 33 adult patients over a 7-week treatment period including ANAVEX<sup>®</sup>2-73 specific precision medicine biomarkers. Based upon the input from the successful U.S. Phase 2 Rett syndrome trial (ANAVEX<sup>®</sup>2-73-RS-001), we updated the endpoints for the AVATAR trial (ANAVEX<sup>®</sup>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, Anxiety, Depression, and Mood Scale (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<sup>®</sup>2-73 were also well tolerated with good medication compliance. All patients who participated in the trial were eligible to receive ANAVEX<sup>®</sup>2-73 under a voluntary open label extension protocol and subsequent Compassionate Use Program.

The very first trial of ANAVEX<sup>®</sup>2-73 in pediatric Rett syndrome patients, the EXCELLENCE trial, completed enrollment in February 2023. This randomized, double-blind, placebo-controlled Phase 2/3 trial in pediatric patients with Rett syndrome included trial sites in Canada, Australia, and the United Kingdom. 92 pediatric patients with Rett syndrome between the ages of 5 through 17 years were treated daily with up to 30 mg ANAVEX<sup>®</sup>2-73. Participants were randomized 2:1 (ANAVEX<sup>®</sup>2-73:placebo) for 12 weeks, followed by a week 16 safety visit and topline results from this trial were announced in early January 2024.

After 12 weeks, the study showed improvement on the key co-primary endpoint RSBQ, which is a detailed 45-item questionnaire for assessing multiple Rett syndrome characteristics by the patients' caregivers. The other co-primary endpoint, the CGI-I, which represents a less granular assessment by the site investigators using a seven-point scoring (one="very much improved" to seven="very much worse"), was not met.

In an ad-hoc analysis, using the predefined mixed-effect model for repeated measure (MMRM) method, after 12 weeks of treatment, ANAVEX®2-73-treated patients improved LS Mean (SE) -12.93 (2.150) points on their RSBQ total score compared to LS Mean (SE) -8.32 (2.537) points in placebo-treated patients. The LS Mean difference (SE) of -4.61 (2.439) points between treated and placebo groups did not reach statistical significance (n=77; p=0.063). ANAVEX®2-73-treated patients demonstrated a rapid onset of action with improvements at 4 weeks after treatment with a RSBQ total score LS Mean (SE) -10.32 (2.086) points in the drug-treated group compared to a LS Mean (SE) -5.67 (2.413) points in placebo-treated patients. The LS Mean difference of -4.65 (2.233) points between treated and placebo groups was statistically significant (n=77; p=0.041).

The key secondary endpoint, the ADAMS, trended favorably. In the same analysis, scores for all RSBQ and ADAMS subscales improved over the course of the study. Collectively, the RSBQ and ADAMS demonstrated improvements in multiple areas, impacting positively in particular repetitive movements, nighttime disruptive behaviors, and social avoidance.

A preliminary review of the safety results indicates there were no new safety signals in the EXCELLENCE study, reinforcing the favorable and manageable safety profile observed with ANAVEX®2-73 to date.

All patients who participated in the trial were eligible to receive ANAVEX®2-73 under a voluntary open label extension protocol, which was completed in June 2024.

A high enrollment rate in the Open Label Extension ("OLE") of over 91% and the high level of requests for the Compassionate Use Program (93%) provide solid numerical evidence for the reported positive Real World Evidence (RWE) from patients with Rett syndrome under Compassionate Use Authorization. Families whose children were previously on drug or placebo in the placebo-controlled trial commented favorably on the improvement of their child's daily life due to ANAVEX®2-73 treatment in the Compassionate Use Program.

### *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 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 ("MDS-UPDRS") 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.

A 48-week OLE ANAVEX2-73-PDD-EP-001 Phase 2 trial was offered to participants after completion of the double-blind placebo-controlled ANAVEX2-73-PDD-001 Phase 2 trial discussed above. The OLE trial assessed safety, tolerability and efficacy, measuring among others, MDS-Unified Parkinson's Disease Rating Scale Parts I, II, III, REM Sleep Behavior Disorder Screening Questionnaire (RBDSQ), CGI-I, as well as cognitive efficacy endpoint Montreal Cognitive Assessment (MoCA) over a 48-week period.

In March 2023, we reported the preliminary ANAVEX2-73-PDD-EP-001 OLE trial data, which demonstrated longitudinal beneficial effects of ANAVEX®2-73 on the pre-specified primary and secondary objectives. Preliminary analysis reveals that ANAVEX®2-73 was found to be generally safe and well tolerated, and safety findings in this trial were consistent with the known safety profile of ANAVEX®2-73. In respect to efficacy, across all efficacy endpoints, patients performed better while on ANAVEX®2-73. While all patients were on drug holiday due to COVID-19 between the DB EOT and the OLE Baseline, the respective efficacy endpoints, including the MDS-UPDRS Part II + III and CGI-I, measured at the end of trial of the double-blind study (DB EOT) and the OLE Baseline, were worsening, as expected in a progressive disease like Parkinson's. However, when patients resumed daily oral ANAVEX®2-73 treatment, a consistent improvement was observed during the extension phase from OLE Baseline through OLE Week 24, and OLE Week 48, respectively. These results are consistent with the pattern observed for all efficacy measures in the extension phase. The two endpoints, MDS-UPDRS Part II + III and CGI-I measured in this study are the planned primary and key secondary endpoints in our forthcoming >6-month Parkinson's disease study.

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 including in people with Parkinson's disease.

### *Schizophrenia, Frontotemporal Dementia and Alzheimer's disease*

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.

In October 2023 a peer-reviewed publication in the journal *Neurobiology of Aging*, titled '*Early treatment with an M1 and sigma-1 receptor agonist prevents cognitive decline in a transgenic rat model displaying Alzheimer-like amyloid pathology*', featured the orally available small molecule ANAVEX®3-71 (AF710B). The preclinical study described the potential disease-modifying properties of ANAVEX®3-71 on Alzheimer's disease pathology as a possible drug candidate for a potential once daily oral preventive strategy for Alzheimer's disease.

In January 2024, in another peer-reviewed publication in the journal *Clinical Pharmacology in Drug Development*, entitled, '*Population-Based Characterization of the Pharmacokinetics and Food Effect of ANAVEX3-71, a Novel Sigma-1 Receptor and Allosteric M1 Muscarinic Receptor Agonist in Development for Treatment of Frontotemporal Dementia, Schizophrenia, and Alzheimer Disease*', reported the population-based characterization of the PK and food effect of ANAVEX®3-71 as part of the single ascending dose study in healthy participants with the primary objective of assessing dose proportionality of ANAVEX®3-71, and to characterize the effect of food on the PK of ANAVEX®3-71. The results from this PK evaluation demonstrated that ANAVEX®3-71, at single ascending doses of 5 to 200 mg, is linear, dose proportional, and time invariant. Food had no effect on the PK of ANAVEX®3-71. This data also expands the safety objectives met in this first-in-human study of ANAVEX®3-71, further supporting its drug development program.

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.



In March 2024, we commenced the U.S. FDA-cleared ANAVEX®3-71-SZ-001 clinical trial: a double-blind, placebo-controlled Phase 2 trial in schizophrenia. The trial consists of two parts to explore multiple ascending doses in individuals with schizophrenia followed by a 28-day treatment period in a larger cohort. The trial will utilize standard clinical outcome measures for schizophrenia including the Positive and Negative Symptoms Scale (PANSS), and novel fluid and electrophysiological biomarkers will also be assessed, leveraging several advances in electroencephalography/event-related potential (EEG/ERP) biomarkers in schizophrenia developed in collaboration with the industry-led ERP Biomarker Qualification Consortium. In addition to the electrophysiological biomarkers, we are also applying novel neuroinflammatory, metabolomic, and transcriptomic biomarkers at the intersection of schizophrenia pathophysiology and ANAVEX®3-71's novel, dual mechanism of action.

Preliminary results from Part A of the ANAVEX®3-71-SZ-001 clinical trial, consisting of a multiple ascending dose study in 16 participants, demonstrated a dose-dependent effect of ANAVEX®3-71 on two key EEG biomarkers in patients with schizophrenia. The effects were most pronounced in the higher dose group indicating a dose-dependent pharmacodynamic effect. The observed changes reversed known electroencephalography (EEG) and ERP biomarker abnormalities associated with schizophrenia. These EEG biomarkers correlate with positive, negative, and cognitive symptoms of schizophrenia.

The currently ongoing Part B of the placebo-controlled Phase 2 study, which includes more participants and a longer treatment duration, will provide more comprehensive data on the efficacy and safety of ANAVEX®3-71 in schizophrenia.

### ***Our Pipeline***

Our research and development pipeline includes ANAVEX®2-73 currently in three different clinical trial indications, and ANAVEX®3-71 currently in one clinical trial 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 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 regulatory authorities 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 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.

We believe preclinical data from our studies also supports further research into the use of 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 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 mice. 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 preclinical 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, may 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 and oligodendrocyte precursor cells (“OPCs”), 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 an orally available 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 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 – Schizophrenia, Frontotemporal Dementia and Alzheimer’s disease*.

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.

The first of these trials, the ANAVEX®3-71-SZ-001 clinical trial, commenced in March 2024 and is more fully described above under *Clinical Trials Overview – Schizophrenia*.

## **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 sigma-1 receptors 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 2024, an estimated 6.9 million Americans are suffering from Alzheimer's disease according to the Alzheimer's Association®. The Alzheimer's Association® estimates that the annual number of new cases of Alzheimer's and other dementias is projected to double by 2050. 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 that 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 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 \$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.
- **Schizophrenia** - Schizophrenia is a persistent and often disabling mental illness impacting how a person thinks, feels, and behaves, and affects nearly 24 million people worldwide, including 2.8 million people in the U.S., according to the World Health Organization. It is characterized by three symptom domains: positive symptoms (hallucinations and delusions), negative symptoms (difficulty enjoying life and withdrawal from others), and cognitive impairment (deficits in memory, concentration, and decision-making). In part due to limitations with current treatments, people living with schizophrenia often struggle to maintain employment, live independently, and manage relationships. While current treatments can be effective in managing select symptoms, approximately 34% of people do not respond to therapy, with an additional 50-60% experiencing only a partial improvement in symptoms or unacceptable side effects.
- **Fragile X** – Fragile X syndrome (FXS) is the most prevalent genetic form of intellectual disability and autism spectrum disorder, primarily affecting boys. As with most neurodevelopmental disorders, FXS is considered a condition of synaptic development and function. The disease has a range of clinical presentations depending on the specific genetic changes associated with an “expansion” of the FMR1 gene. The disease is characterized by deficits in long-term potentiation and homeostatic plasticity. FXS has been detected in all populations and ethnic groups. Researchers do not know the exact number for how many Americans could have full mutation FXS. Studies estimate that the disease affects approximately 1:4,000 males and 1:6,000 females. Worldwide, more than 1,400,000 people could be affected by FXS.
- **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 medications that are 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 to \$3.7 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 twenty-five (25) U.S. patents, twenty-five (25) 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,” which 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 one issued U.S. patent entitled “A2-73 crystalline polymorph compositions of matter and methods of use thereof”. It claims crystals of A2-73 freebase or its fumarate salt, dosage forms and pharmaceutical formulations. This patent is expected to expire in July 2039, absent any patent term extension for regulatory delays.

We own four issued U.S. patents each with claims directed to crystalline forms of ANAVEX®2-73. The first of these four 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 four 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 2036, absent any patent term extension for regulatory delays. The third of these four 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 2036, absent any patent term extension for regulatory delays. The fourth of these four patents

claims method of making certain crystalline forms ANAVEX®2-73. This patent is expected to expire in October 2036, absent any patent term extension for regulatory delays.

We also own three issued U.S. patents for seizure treatment. The first of these three 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 three 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. The third of these three patents claims a dosage form for seizure reduction, comprising (i) ANAVEX®19-144, (ii) ANAVEX®2-73, or (iii) a combination of ANAVEX®19-144 and ANAVEX®2-73; and optionally further comprising a low-dose anti-epilepsy drug. All three patents are expected to expire in October 2035, absent any patent term extension for regulatory delays.

We also own four issued U.S. patents with claims directed to treating neurodevelopmental disorders. These patents claim methods for treating a neurodevelopmental disorder, multiple sclerosis, their related biochemical and functional abnormalities, or loss-of-function associated with a neurodevelopmental disorder, by 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 four 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 two issued U.S. patent for the treatment of insomnia, anxiety, or agitation. The first of the two patents claims 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. The second of the two patents claims a dosage form comprising any of, or any combination of ANAVEX®2-73, ANAVEX®19-144, and/or ANAVEX®1-41. This patent is expected to expire in July 2038, absent any patent term extension for regulatory delays.

Further, we own one issued U.S. patent with claims directed to a method of treating systolic hypertension using ANAVEX®2-73. This patent is expected to expire in July 2039, absent any patent term extension for regulatory delays. Additionally, we own one issued U.S. patent with claims directed to pharmaceutical dosage forms of (-) enantiomer of ANAVEX®2-73. This patent is expected to expire in July 2036, absent any patent term extension for regulatory delays.

We also own three (3) issued U.S. patents related to ANAVEX®1066. The first of these three 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. The third patent claims dosage forms and pharmaceutical compositions comprising (+) ANAVEX®1066 isomer. All three 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 and certain granted foreign patents 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" in Part I, Item 1A of this Annual Report on Form 10-K.

### ***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 clinical trials, the parameters to be used in monitoring the safety of the trial, and the effectiveness criteria to be evaluated should the trial include 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](http://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 the 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 the 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 the 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, as, 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 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 2024 and 2023.

### ***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 forty-two 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](http://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 there free of charge. 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**

### **Risk Factor Summary**

The following is a summary of the risks and uncertainties that could cause our business, financial condition or operating results to be harmed. We encourage you to carefully review the full risk factors contained in this report in their entirety for additional information regarding these risks and uncertainties.

- Our history of losses and no revenue raises a risk regarding our ability to continue as a going concern in the future;
- We have a very limited relevant operating history upon which an evaluation of our performance and prospects can be made. We may never be able to successfully develop marketable products or generate any revenue. If we cannot generate sufficient revenues, we may suspend or cease operations;
- Our research and development plans will require substantial additional future funding. We may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our research and development activities;
- 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;
- Even if our products are approved, we may not be able to generate significant revenues from or successfully commercialize them, 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;
- Our research and development plans require substantial additional future funding which could impact our operations and financial condition;
- If we or any companion diagnostic collaborator of ours are unable to timely develop and obtain regulatory approval for companion diagnostic tests for our drug candidates, we may not realize the commercial potential of our drug candidates;
- The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable, which could lead to our inability to generate product revenue;
- Regulatory authorities may not accept data from our trials conducted outside the United States;
- Fast Track designation or breakthrough therapy designation that we have received or may seek out may not actually lead to a faster FDA review and approval process;
- We may be unable to maintain any benefits associated with orphan drug designation, including market exclusivity;

- 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;
- If a particular product candidate causes undesirable side effects, then we may be unable to receive regulatory approval of or commercialize such product candidate;
- We are highly dependent on our key personnel and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy;
- 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 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;
- None of our potential drug compounds may reach the commercial market and our business may fail;
- Material modifications in the methods of product candidate manufacturing may result in additional costs or delay;
- Our technologies and future products may be rendered undesirable or obsolete 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;
- 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;
- Our reliance on third parties 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;
- If we fail to compete with respect to partnering, licensing, mergers, acquisitions, joint venture and other collaboration opportunities, our ability to research and develop our potential drug compounds may be limited;
- The use of any of our products in clinical trials may expose us to liability claims, 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;
- Continuing regulatory obligations and ongoing regulatory review may result in additional expense. Our compounds could be subject to restrictions on marketing or withdrawal from the market, and we may be subject to penalties when and if any of them are approved;
- Changes in funding for the FDA, the SEC and other government agencies could prevent these agencies from performing normal functions on which the operations of our business may rely, which could negatively affect our business;
- We receive Australian government research and development income tax incentive refunds. Loss of access to such incentives could have a negative effect on our future cash flows and the funding of future research and development projects;
- Operating our business internationally carries various risks which could materially adversely affect our business;
- Our ability to use our net operating loss carryforwards and tax credit carryforwards may be subject to limitation;
- Healthcare laws and regulations could expose us to criminal sanctions, civil and administrative penalties, contractual damages, reputational harm and diminished profits and future earnings, among other penalties;
- 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;

- 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;
- Issuing additional shares of common stock will result in the dilution of our existing stockholders and may cause our stock price to fall. A decline in our stock price could affect our ability to raise further working capital and adversely affect our operations. Raising funds at lower prices would severely dilute existing or future investors;
- Our stock price has been volatile and may be volatile in the future and our common stock may become the target of a “short squeeze”;
- 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. Our disclosure controls and procedures may not prevent or detect all errors or acts of 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;
- Patent terms may be inadequate to protect our competitive position on our product candidates. If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, our competitors could develop and commercialize product candidates similar or identical to ours, and our ability to successfully commercialize our product candidates may be impaired;
- If we fail to comply with our obligations in intellectual property licensing agreements or experience disruptions to our business relationships with our licensors, we could lose important intellectual property rights. If we are unable to protect the confidentiality of our trade secrets, our business would be harmed;
- Intellectual property infringement claims may adversely affect our development and commercialization efforts;
- 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;
- We may become involved in lawsuits to protect or enforce our patents or other intellectual property;

Obtaining and maintaining our patent protection depends on compliance with various requirements imposed by governmental patent agencies. Changes in patent law could impair our ability to protect our product candidates; and

- We may fail to protect our intellectual property rights or the confidentiality of our trade secrets. Changes in patent law could diminish the value of our patents and patent applications in general.

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, 2024, we have accumulated a deficit of approximately \$336 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 sale 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, through issuances of shares under the Purchase Agreement with Lincoln Park Capital Fund, LLC (“Lincoln Park”) pursuant to which the Company may direct Lincoln Park to purchase shares of common stock registered under an effective registration statement, or, historically, through draws under our “at-the-market offering” in connection with the Amended and Restated Sales Agreement with Cantor Fitzgerald & Co. and SVB Leerink LLC (the “Sales Agents”), pursuant to which we could offer and sell shares of common stock registered under an effective registration statement from time to time through the Sales Agents. The Company terminated the Sales Agreement in July 2024. 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 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.

***The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable, which could lead to our inability to generate product revenue.***

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates in those countries. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. Our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. Even if we eventually complete clinical testing and receive approval of any regulatory filing for our product candidates, the FDA and comparable foreign regulatory authorities may approve our product candidates for a more limited indication or a narrower patient population than we originally requested. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA or comparable international regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA or comparable international regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and potency and safety in the full population for which we seek approval;
- the FDA or comparable international regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a Biologics License Application, New Drug Application or other submission or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA or comparable international regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or comparable international regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or international foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

In order to market any product candidates outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and potency and approval standards. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, government shutdowns, including as a result of budget delays or other circumstances like the COVID-19 pandemic and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects.

***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 those 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 a particular product candidate causes undesirable side effects, then we may be unable to receive regulatory approval of or commercialize such product candidate.***

We may experience numerous unforeseen events during, or as a result of, the testing process that could delay or prevent commercialization of any of our product candidates, including the occurrence of undesirable side effects. Such side effects could lead to clinical trial challenges, such as difficulties in subject recruitment, retention, and adherence, potential product liability claims, and possible termination by health authorities. These types of clinical trial challenges could in turn, delay or prevent regulatory approval of our product candidate. Side effects may also lead regulatory authorities to require stronger product warnings on the product label, costly post-marketing studies, and/or a REMS, among other possible requirements. If the product candidate has already been approved, such approval may be withdrawn. Any delay in, denial, or withdrawal of marketing approval for one of our product candidates will adversely affect our business, including our results of operations and financial position. Even if one or more of our product candidates receives marketing approval, undesirable side effects may limit such product's commercial viability. Patients may not wish to use our product, physicians may not prescribe our product, and our reputation may suffer. Any of these events may significantly harm our business and financial prospects.

***We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.***

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and an inability to find suitable replacements could result in delays in product development and harm our business.

Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment or service with us on short notice. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel in an extremely competitive market for employees and other service providers.

***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.

***Material modifications in the methods of product candidate manufacturing may result in additional costs or delay.***

As product candidates progress from preclinical studies to late-stage clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, materials and processes, are altered along the way in an effort to optimize yield, manufacturing batch size, minimize costs and achieve consistent purity, identity, potency, quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and could affect planned or other clinical trials conducted with product candidates produced using the modified manufacturing methods, materials, and processes. This could delay completion of clinical trials and could require non-clinical or clinical bridging and comparability studies, which could increase costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates, if approved.

***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 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 such 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 our information systems or data, or those of third parties upon whom we rely, are or were compromised, our business may be adversely affected.***

In the course of our business, we, or third parties upon whom we rely, may gather, collect, receive, use, transmit, store/retain or dispose of data and confidential information (such as confidential employee information or health-related data), sensitive data, intellectual property and trade secrets.

Cyberattacks, malicious internet-based activity, online and offline fraud and other similar activities threaten the confidentiality, integrity, and availability of our sensitive information and information technology systems, and those of the third parties upon whom we rely. We, and the third parties upon whom we may rely, may be subject to a variety of these evolving threats.

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. The existence of a remote workforce also poses increased risks to our information technology systems and data, as more of our employees work from home, utilizing network connections outside our premises.

Any misappropriation, loss or other unauthorized disclosure of confidential information gathered, stored or used by us or by third parties on our behalf, 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.

Our contracts with third parties upon whom we may rely, may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. In addition, we could incur increased litigation as a result of any potential cyber-security breach and our insurance coverage may not be adequate or sufficient in type or amount to protect us from or to mitigate liabilities arising out of our privacy and security practices.

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.

***Changes in funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.***

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees, statutory, regulatory and policy changes, and business disruptions, such as those caused by the COVID-19 pandemic. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough

critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

***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 than 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, 2024, we had approximately \$128.5 million of U.S. federal and \$16.9 million of state and local NOL carryforwards. We had approximately \$16.6 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 Internal Revenue 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, 2024 and 2023, 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 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 ANAVEX®2-73 in its various optical or crystal forms, its therapeutic indications, and dosage forms comprising certain doses of ANAVEX®2-73 combined with another therapeutic agent. We may not be able to obtain broader scope 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 and/or interfering with 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/or 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 could 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 pre-issuance 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 and/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 twenty-two U.S. patents, twenty-three 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 we are 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. We are 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 us 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 a 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 what 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 a 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.

***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 1C. CYBERSECURITY**

### **Risk management and strategy**

We have implemented and maintain various information security processes designed to identify, assess and manage material risks from cybersecurity threats to our cloud networks, third party hosted services, communications systems, hardware and software, and our critical data, including intellectual property, confidential information that is proprietary, strategic or competitive in nature, and data related to our clinical trials and products.

We have processes designed to protect our information systems, data, assets, infrastructure, and computing environments from cybersecurity threats and risks. Our cybersecurity strategy includes the use of third-party IT professionals to assess the effectiveness of our cybersecurity practices for possible cybersecurity threats and to manage our IT systems to mitigate these threats. We also use multi-factor authentication, maintain logical, physical and technical controls designed to deter, prevent, mitigate and respond to cybersecurity threats. Further, we provide periodical cybersecurity reminders to our employees to emphasize the importance of adherence to our security policies. We also carry a separate cybersecurity commercial insurance policy covering the potential financial losses that may occur in the event we experience a cybersecurity incident.

Our assessment and management of material risks from cybersecurity threats are integrated into the Company's overall risk management processes. We conduct organizational risk assessments commensurate with our size and complexity of our operations. We are in a continuous process of reviewing and implementing incremental information technology strategies to mitigate cybersecurity risks as new risks arise and as our operations evolve. This has led us to engage third party professionals to assist in the implementation of processes to manage these risks. We also use third-party service providers across a variety of functions throughout our business, such as application providers, hosting companies, contract research organizations, contract manufacturing organizations, distributors, and supply chain resources. We have a vendor management process to help manage cybersecurity risks associated with our use of certain of these providers. For certain vendors, these processes include a comprehensive vendor audit process.

As of the date of this Annual Report, we do not believe that any past cybersecurity incidents that have been detected have materially affected, or are reasonably likely to materially affect, our business strategy, results of operations, or financial condition.

See "*Risk Factors - Risks Related to Our Business and Operations*" for additional information about the risks to our business associated with cybersecurity or a breach or compromise to our information security systems.

### **Governance**

Our board of directors addresses the Company's cybersecurity risk management as part of its general oversight function. The audit committee of the board of directors is responsible for overseeing the Company's cybersecurity risk management processes, including oversight of mitigation of risks from cybersecurity threats. The audit committee receives periodic reports from senior management concerning the Company's significant cybersecurity threats and risk and the processes the Company has implemented to address them.

Currently we have two cybersecurity experts on our Audit Committee

## **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 \$11,000 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**

The Company is subject to claims and legal proceedings that arise during the course of business. The Company is currently subject to the following lawsuits:

On March 13, 2024, a shareholder class action complaint was filed in the United States District Court for the Southern District of New York. The complaint is captioned *Blum v. Anavex Life Sciences, Corp. et al.*, case number 1:24-cv-01910, and it named the Company and Christopher Missling as Defendants. The complaint alleges violations of the Securities and Exchange Act of 1934 associated with disclosures and statements made with respect to certain clinical trials for ANAVEX<sup>®</sup>2-73 related to Rett syndrome (the “March 2024 Complaint”). At a hearing on or about June 13, 2024, the Court named another purported Company shareholder, Quintessa Huey, as lead plaintiff with respect to the March 2024 Complaint. An Amended Complaint was filed by the appointed lead plaintiff on July 12, 2024, which asserts allegations related to purported violations of Section 10(b) of the Securities Exchange Act tied to disclosures associated with the same clinical trials related to Rett Syndrome, and which names the Company and Christopher Missling as defendants. The Amended Complaint seeks unspecified damages, as well as costs, including counsel and expert witness fees, on behalf of class of investors who purchased stock of the Company on the NASDAQ during the period February 1, 2022 through January 1, 2024. The defendants filed a motion to dismiss the complaint. The motion to dismiss is fully-briefed and awaiting a decision by the Court.

On May 8, 2024, a similar complaint was filed in the same court by Kenneth Downing (case no. 1:2024-cv-03529), a purported shareholder of the Company, against the same defendants as the March 2024 Complaint. The defendants filed a motion to dismiss the complaint. Plaintiff Downing voluntarily dismissed his complaint subsequent to the filing of the motion to dismiss.

On or about May 13, 2024, a derivative lawsuit was filed against the Company (as nominal defendant), Christopher Missling, and members of the Company’s Board of Directors in the U.S. District Court for the District of Nevada by another purported shareholder named Denise Deangelis. The complaint asserts various common law claims (including breach of fiduciary duty) and violation of Section 14(a) of the Securities Exchange Act regarding the same or similar allegations at issue in the two purported class action lawsuits related to disclosures and statements made about certain clinical trials related to Rett Syndrome. The parties are currently due to file a proposed schedule for the anticipated motion to dismiss by the Company and Christopher Missling (the other named defendants have not been served with the complaint) on or before January 15, 2025.

We know of no other material pending legal or governmental proceedings, other than ordinary routine litigation incidental to our business, to which our Company or our subsidiaries are a party or of which any of their property is subject. There are no other proceedings in which any of our directors, officers or affiliates, or any registered or beneficial stockholder holding more than 5% of our shares, or any associate of such persons, is an adverse party or has a material interest adverse to our or our subsidiaries’ 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 December 23, 2024, there were approximately 48 stockholders of record, and 84,815,517 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, 2024, 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.

### ***Financial Operations 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 studies 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 studies. Personnel costs include salaries and wages, benefits, and non-cash share-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 share-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.

### **Comparison of year ended September 30, 2024 to year ended September 30, 2023**

#### ***Operating Expenses***

Our operating expenses for fiscal 2024 decreased to \$52.9 million, from \$55.8 million in fiscal 2023. The decrease is attributable to a modest decrease in research and development expenses of \$1.9 million (4.3%) to \$41.8 million in fiscal 2024 as well as a small decrease in general and administrative expenses of \$1.0 million (8.3%) to \$11.0 million in fiscal 2024, as more fully described below.

During fiscal 2024, we experienced an overall decrease in total research and development expenses over the comparable fiscal 2023 financial year.

The decreases were largely due to:

- (i) a decrease in share-based compensation expense of \$5.0 million as a result of the vesting of previous option awards and a change in estimated vesting dates associated with performance-based option awards;
- (ii) a decrease of approximately \$3.5 million relating to our Rett syndrome program as a result of the completion of the EXCELLENCE trial and the respective open label extension; and
- (iii) a decrease of approximately \$1.2 million in expenditures over the comparable period relating to our Alzheimer's program, as a result of the completion of the Phase 2b/3 clinical trial and its related open label extension.

These decreases were largely offset by the following increases in research and development expenditures over the comparable fiscal 2023 financial year:

- (i) an increase in personnel costs of \$3.4 million related to the addition of new employees including new additions to the Company's leadership team, and expenses related to the engagement of consultants to assist in the preparation of the submission of our Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA);
- (ii) an increase of approximately \$3.6 million over the comparable period relating to manufacturing activities of ANAVEX®2-73 for potential commercial use, and to support the MAA; and
- (iii) an increase of \$2.2 million over the comparable period relating to expenditures on the ANAVEX®3-71-SZ-001 clinical trial, which trial commenced in the second quarter of fiscal 2024.

The following table summarizes our research and development expenses for the years ended September 30, 2024, and 2023 (in thousands):

	<b>2024</b>	<b>2023</b>
Costs of external service providers .....	\$ 21,974	\$ 22,542
Personnel costs.....	13,676	10,264
Share-based compensation.....	5,813	10,812
Other common costs .....	375	99
Total research and development costs.....	<u>\$ 41,838</u>	<u>\$ 43,717</u>

External service provider cost by product candidate was as follows (in thousands):

	<b>2024</b>	<b>2023</b>
ANAVEX®2-73 .....	\$ 17,572	\$ 19,540
ANAVEX®3-71 .....	3,748	2,624
All other product candidates .....	150	6
Other external service provider costs.....	504	372
Total external service provider costs.....	<u>\$ 21,974</u>	<u>\$ 22,542</u>

General and administrative expenses were \$11.0 million for the fiscal 2024 financial year, as compared to \$12.0 million in fiscal 2023. The primary reason for the decrease in general and administrative expenses was a reduction in share-based compensation charges of \$1.9 million, as a result of the vesting of previous option awards and the extended timeline of milestone based vesting awards.

We expect to see our research and development expenditures increase from current levels as we advance our clinical programs, including continuation of ANAVEX®3-71 trial in Schizophrenia and subsequent advancements, planned advancement of ANAVEX®2-73 for Parkinson's disease, planned initiation of an ANAVEX®2-73 for a Fragile X clinical trial, and as we continue to grow our staffing to manage and support these clinical initiatives.

#### ***Other income (net)***

Net other income for the year ended September 30, 2024 was \$9.9 million as compared to \$8.3 million for fiscal 2023. The primary reason for the increase in other income was due to a one-time financing charge of \$0.9 million recognized in the comparable year associated with entering into the 2023 Purchase Agreement (as described below), as well as an increase in interest income in fiscal 2024 earned on cash and cash equivalents, due to an increase in market wide interest rates year over year.

During fiscal 2024, we recorded \$2.3 million in research and development incentive income, consisting of the Australian

research and development incentive credit administered through the ATO, in connection with fiscal 2024 eligible expenditures. In comparison, research and development incentive income for fiscal 2023 was \$2.7 million in connection with fiscal 2023 eligible expenditures. This income is driven by the clinical trial expenditures incurred in Australia, and the decrease is a result of the completion of the EXCELLENCE trial in Rett Syndrome and the Phase 2b/3 clinical trial in Alzheimer's disease, as well as related open label extension trials, which were completed during fiscal 2024. We expect to continue to receive support from the Australian government for future clinical trials which we plan to conduct, in part, within Australia.

### ***Net loss***

Net loss for fiscal 2024 was \$43.0 million, or \$0.52 per share, compared to a net loss of approximately \$47.5 million, or \$0.60 per share for fiscal 2023.

## **Liquidity and Capital Resources**

### ***Working Capital (in thousands)***

	<b>2024</b>	<b>2023</b>
Current Assets .....	\$ 135,567	\$ 154,386
Current Liabilities .....	15,304	12,534
Working Capital .....	<u>\$ 120,263</u>	<u>\$ 141,852</u>

At September 30, 2024, we had \$132.2 million in cash and cash equivalents, a decrease from \$151.0 million at September 30, 2023.

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***

Following is a summary of sources of cash flows for the years ended September 30, 2024 and 2023 (in thousands)

	<b>2024</b>	<b>2023</b>
Cash flows used in operating activities.....	\$ (30,812)	\$ (27,785)
Cash flows provided by financing activities .....	11,975	29,651
(Decrease) increase in cash.....	\$ (18,837)	\$ 1,866

### ***Cash flow used in operating activities***

There was an increase in cash used in operating activities of \$3.0 million during fiscal 2024. The principal reason for this is an increase in net cash expenses, after taking into account non-cash share-based compensation, over the comparable period of approximately \$3.3 million.

### ***Cash flow provided by financing activities***

Cash provided by financing activities in fiscal 2024 was \$12.0 million, comprised of \$11.3 attributable to cash received from the issuance of common shares at various market prices under the 2023 Purchase Agreement (as defined below) and \$0.7 million received pursuant to the exercise of stock options.

Cash provided by financing activities in fiscal 2023 was \$29.7 million, comprised of \$27.9 million attributable to cash received from the issuance of common shares under the 2023 Purchase Agreement and \$1.8 million received pursuant to the exercise of stock options.

## **Other Financings**

### **2023 Purchase Agreement**

On February 3, 2023, the Company entered into a \$150,000,000 purchase agreement (the "2023 Purchase Agreement") with Lincoln Park Capital Fund, LLC ("Lincoln Park"), pursuant to which the Company has the right to sell and issue to Lincoln Park, and Lincoln Park is obligated to purchase, up to \$150.0 million in value of its shares of Common Stock from time to time over a three-year period until February 3, 2026.



On any business day and subject to certain customary conditions, the Company may direct Lincoln Park to purchase up to 200,000 shares of Common Stock (such purchases, “Regular Purchases”). The amount of a Regular Purchase may increase under certain circumstances based on the market price of the Common Stock; provided, however, that Lincoln Park’s committed obligation under any Regular Purchase shall not exceed \$4.0 million. The purchase price of shares of Common Stock will be based on the then prevailing market prices of such shares at the time of sales as described in the 2023 Purchase Agreement. There are no limits on the price per share that Lincoln Park may pay to purchase Common Stock under the 2023 Purchase Agreement. In addition, if the Company has directed Lincoln Park to purchase the full amount of Common Stock available as a Regular Purchase on a given day, it may direct Lincoln Park to purchase additional amounts as “accelerated purchases” and “additional accelerated purchases,” each as set forth in the 2023 Purchase Agreement.

The 2023 Purchase Agreement limits the Company’s sale of shares of Common Stock to Lincoln Park to 15,606,426 shares of Common Stock, representing 19.99% of the shares of the Common Stock outstanding on the date of the 2023 Purchase Agreement unless (i) stockholder approval is obtained to issue more than such amount or (ii) the average price of all applicable sales of Common Stock to Lincoln Park under the 2023 Purchase Agreement equals or exceeds the lower of (A) the closing price of the Common Stock on the Nasdaq Capital Market immediately preceding the Execution Date or (B) the average of the closing price of the Common Stock on the Nasdaq Capital Market for the five Business Days immediately preceding the Execution Date.

The 2023 Purchase Agreement also prohibits the Company from directing Lincoln Park to purchase any shares of Common Stock if those shares, when aggregated with all other shares of Common Stock then beneficially owned by Lincoln Park and its affiliates, would result in Lincoln Park and its affiliates having beneficial ownership, at any single point in time, of more than 4.99% of the then total outstanding shares of Common Stock, as calculated pursuant to Section 13(d) of the Securities Exchange Act of 1934, as amended, and Rule 13d-3 thereunder.

In consideration for entering into the 2023 Purchase Agreement, the Company issued to Lincoln Park 75,000 shares of Common Stock as a commitment fee (the “initial commitment shares”) during the year ended September 30, 2023 and agreed to issue up to 75,000 shares pro rata (collectively with the initial commitment shares, the “commitment shares”), when and if, Lincoln Park purchased, at the Company’s discretion, the \$150.0 million aggregate commitment.

During the year ended September 30, 2024, the Company issued to Lincoln Park an aggregate of 2,455,646 shares of Common Stock under the 2023 Purchase Agreement, including 2,450,000 shares of Common Stock for an aggregate purchase price of \$11.3 million and 5,646 commitment shares. During the year ended September 30, 2023, the Company issued to Lincoln Park an aggregate of 3,288,943 shares of Common Stock under the 2023 Purchase Agreement, including 3,275,000 shares of Common Stock for an aggregate purchase price of \$27.9 million and 13,943 commitment shares as well as the 75,000 initial commitment shares.

On September 30, 2024, an amount of \$110.8 million remained available under the 2023 Purchase Agreement.

### **Controlled Equity Offering Sales Agreement**

On May 1, 2020, we entered into an Amended and Restated Sales Agreement (the “2020 Sales Agreement”) with Cantor Fitzgerald & Co. and SVB Leerink LLC (the “Sales Agents”), pursuant to which we could 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”).

No shares were sold during the years ended September 30, 2024 and 2023 under the 2020 Sales Agreement. The Company terminated the 2020 Sales Agreement on July 24, 2024.

### ***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 share-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 share-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.

### *Share-based Compensation*

We account for all share-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 share-based payments with graded vesting are recognized on a straight-line basis. Share-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**

Not required for smaller reporting companies.

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

**ANAVEX LIFE SCIENCES CORP.**  
**CONSOLIDATED FINANCIAL STATEMENTS**  
September 30, 2024

## 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 sheets of Anavex Life Sciences Corp. (a Nevada corporation) and subsidiaries (the “Company”) as of September 30, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, changes in stockholders’ equity, and cash flows for each of the two years in the period ended September 30, 2024, and the related notes (collectively referred to as the “financial statements”). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of September 30, 2024 and 2023, and the results of its operations and its cash flows for each of the two years in the period ended September 30, 2024, in conformity with accounting principles generally accepted in the United States of America.

### Basis for opinion

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

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

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

### 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) relate 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.

Melville, New York  
December 23, 2024



Anavex Life Sciences Corp.  
Consolidated Balance Sheets  
(in thousands, except share and per share amounts)

	September 30,	
	<u>2024</u>	<u>2023</u>
Assets .....		
Current .....		
Cash and cash equivalents .....	\$ 132,187	\$ 151,024
Incentive and tax receivables .....	2,449	2,709
Prepaid expenses and other current assets .....	931	653
Total Assets .....	<u>\$ 135,567</u>	<u>\$ 154,386</u>
Liabilities and Stockholders' Equity .....		
Current Liabilities .....		
Accounts payable .....	\$ 9,627	\$ 4,322
Accrued liabilities - Note 3 .....	4,835	7,295
Deferred grant income - Note 4 .....	842	917
Total Liabilities .....	<u>\$ 15,304</u>	<u>\$ 12,534</u>
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:.....		
84,795,517 common shares (2023 - 82,066,511).....	85	82
Additional paid-in capital .....	456,249	434,839
Accumulated deficit .....	(336,071)	(293,069)
Total Stockholders' Equity .....	<u>\$ 120,263</u>	<u>\$ 141,852</u>
Total Liabilities and Stockholders' Equity .....	<u>\$ 135,567</u>	<u>\$ 154,386</u>

See Accompanying Notes to Consolidated Financial Statements

Anavex Life Sciences Corp.  
Consolidated Statements of Operations and Comprehensive Loss  
(in thousands, except share and per share amounts)

	Years Ended September 30, 2024	2023
<b>Operating expenses</b> .....		
General and administrative .....	\$ 11,039	\$ 12,039
Research and development .....	<u>41,838</u>	<u>43,717</u>
Total operating expenses .....	<u>52,877</u>	<u>55,756</u>
Operating loss .....	(52,877)	(55,756)
<b>Other income (expense)</b> .....		
Grant income .....	75	25
Research and development incentive income .....	2,291	2,718
Interest income, net .....	7,320	6,519
Other financing expense .....	—	(964)
Foreign exchange gain (loss) .....	<u>189</u>	<u>(40)</u>
Total other income, net .....	<u>9,875</u>	<u>8,258</u>
Net loss before provision for income taxes .....	(43,002)	(47,498)
Income tax expense, current .....	<u>—</u>	<u>(7)</u>
Net loss and comprehensive loss .....	\$ (43,002)	\$ (47,505)
Net Loss per share .....		
Basic and diluted .....	<u>\$ (0.52)</u>	<u>\$ (0.60)</u>
Weighted average number of shares outstanding .....		
Basic and diluted .....	<u>83,468,049</u>	<u>79,787,596</u>

See Accompanying Notes to Consolidated Financial Statements

Anavex Life Sciences Corp.  
Consolidated Statements of Cash Flows  
(in thousands, except share and per share amounts)

	<b>Years ended September 30,</b> <b>2024</b>	<b>2023</b>
<b>Cash Flows used in Operating Activities</b> .....		
Net loss.....	\$ (43,002)	\$ (47,505)
Adjustments to reconcile net loss to net cash used in operations: .....		
Non-cash financing related charges .....	—	845
Share-based compensation.....	9,438	16,370
Changes in working capital balances related to operations: .....		
Incentive and tax receivables .....	260	484
Prepaid expenses and deposits .....	(278)	(299)
Accounts payable .....	5,305	497
Accrued liabilities .....	(2,460)	1,350
Deferred grant income .....	(75)	473
Net cash used in operating activities.....	<u>(30,812)</u>	<u>(27,785)</u>
<b>Cash Flows provided by Financing Activities</b> .....		
Issuance of common shares .....	11,284	27,875
Proceeds from exercise of stock options.....	691	1,776
Net cash provided by financing activities .....	<u>11,975</u>	<u>29,651</u>
(Decrease) Increase in cash and cash equivalents during the year .....	(18,837)	1,866
Cash and cash equivalents, beginning of year .....	151,024	149,158
<b>Cash and cash equivalents, end of year</b> .....	<u><u>\$ 132,187</u></u>	<u><u>\$ 151,024</u></u>
<b>Supplemental Cash Flow Information</b> .....		
Cash paid for state and local franchise taxes .....	<u><u>\$ 300</u></u>	<u><u>\$ 136</u></u>

See Accompanying Notes to Consolidated Financial Statements

Anavex Life Sciences Corp.  
Consolidated Statements of Changes in Stockholders' Equity  
(in thousands, except share and per share amounts)

	<u>Common Stock</u>		<u>Additional</u>	<u>Accumulated</u>	
	<u>Shares</u>	<u>Par Value</u>	<u>Paid-in</u>	<u>Deficit</u>	<u>Total</u>
			<u>Capital</u>		
<b>Balance, October 1, 2022 .....</b>	<b>77,942,815</b>	<b>\$ 78</b>	<b>\$ 387,977</b>	<b>\$ (245,564)</b>	<b>\$ 142,491</b>
Shares issued under 2023 Purchase Agreement.....					
Initial Commitment shares .....	75,000	—	845	—	845
Purchase shares .....	3,275,000	3	27,872	—	27,875
Commitment shares .....	13,943	—	—	—	—
Shares issued pursuant to exercise of stock options	759,753	1	1,775	—	1,776
Share based compensation .....	—	—	16,370	—	16,370
Net loss.....	—	—	—	(47,505)	(47,505)
<b>Balance, September 30, 2023.....</b>	<b>82,066,511</b>	<b>82</b>	<b>434,839</b>	<b>(293,069)</b>	<b>141,852</b>
Shares issued under 2023 Purchase Agreement.....					
Purchase shares .....	2,450,000	3	11,281	—	11,284
Commitment shares .....	5,646	—	—	—	—
Shares issued pursuant to exercise of stock options	273,360	—	691	—	691
Share based compensation .....	—	—	9,438	—	9,438
Net loss.....	—	—	—	(43,002)	(43,002)
<b>Balance, September 30, 2024.....</b>	<b>84,795,517</b>	<b>\$ 85</b>	<b>\$ 456,249</b>	<b>\$ (336,071)</b>	<b>\$ 120,263</b>

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 trials to identify biomarkers, which are used in the analysis of its clinical trials for the treatment of neurodegenerative and neurodevelopmental diseases.

The Company’s focus is on developing innovative treatments for Alzheimer’s disease, Parkinson’s disease, schizophrenia, neurodevelopmental, neurodegenerative, and rare diseases, including Rett syndrome, and other central nervous system (CNS) disorders.

### **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 sales to pharmaceutical companies or generate commercial revenues. To date, we have not generated any revenue from our operations. The Company expects the business to continue to experience negative cash flows from operations for the foreseeable future and cannot predict when, if ever, our 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 are 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 2023 Purchase 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.

## **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 and tax receivables, 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 carrying 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, 2024 and 2023, 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 share-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 trials and 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, through its wholly owned subsidiary Anavex Australia, 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”). The Australia R&D credit program provides for a cash refund based on a percentage of eligible research and development activities undertaken in Australia by 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 at a rate of 18.5% above the claimant’s company tax rate in Australia.

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.

### ***License Fees***

The Company expenses amounts paid to acquire licenses associated with products under development when the ultimate recovery of the amounts paid is uncertain and the technology has no alternative future use when acquired. Acquisitions of technology licenses are charged to expense or capitalized based on management’s assessment regarding the ultimate recoverability of the amounts paid and the potential for alternative future use. The Company has determined that the technological feasibility for its product candidates is reached when the requisite regulatory approvals are obtained to make the product available for sale.

### ***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, 2024, diluted loss per share excludes 15,047,754 potentially dilutive common shares (2023 – 14,271,780) 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 statements of operations and comprehensive loss in the period they are earned, typically 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 and comprehensive loss.

The Company recognizes interest and penalties related to current income tax expense on the interest income, net line, in the accompanying consolidated statements of operations and comprehensive loss. Accrued interest and penalties, if any, are included in accrued liabilities on the consolidated balance sheets.

### ***Share-based Compensation***

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

The fair value of all share-based payments 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 share-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-based awards 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 sufficient 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 share-based compensation awards may be paid in cash or, if approved by the Company's compensation committee (or in the case of warrants by the Board of Directors) in advance, "net settled" in shares of the Company's common stock. In a net settlement of an share-based award, 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 award 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 instrument 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, 2024 and 2023, the Company did not have any Level 2 or Level 3 assets or liabilities.

### ***Recently Adopted Accounting Pronouncements***

On October 1, 2022, the Company adopted Accounting Standards Update (ASU) 2021-10, Government Assistance (Topic 832) – Disclosures by Business Entities about Government Assistance, which requires business entities to disclose information about transactions with a government that are accounted for by applying a grant or contribution model by analogy. For transactions within scope, the new standard requires the disclosure of information about the nature of the transaction, including significant terms and conditions, as well as the amounts and specific financial statement line items affected by the transaction. The disclosure of the Company’s research and development tax incentive income and receivable is detailed in Note 4.

### ***Recent Accounting Pronouncements***

In November 2023, the Financial Accounting Standards Board (FASB) issued ASU No. 2023-07, “Segment Reporting: Improvements to Reportable Segment Disclosures.” This guidance requires disclosure of incremental segment information on an annual and interim basis. This amendment is effective for our fiscal year ending September 30, 2025 and our interim periods within the fiscal year ending September 30, 2026. The Company is currently assessing the impact of this guidance on its disclosures.

In December 2023, the FASB issued ASU No. 2023-09, “Income Taxes: Improvements to Income Tax Disclosures.” This guidance requires consistent categories and greater disaggregation of information in the rate reconciliation and disclosures of income taxes paid by jurisdiction. This amendment is effective for our fiscal year ending September 30, 2026. The Company is currently assessing the impact of this guidance on its disclosures.

### **Note 3 Accrued Liabilities**

The principal components of accrued liabilities consist of (in thousands):

	September 30,	
	2024	2023
Accrued investigator payments.....	\$ 860	\$ 2,006
Accrued compensation and benefits.....	1,527	1,360
Fixed contract accruals .....	—	38
Milestone-based contract accruals .....	557	1,267
All other accrued liabilities.....	1,891	2,624
<b>Total accrued liabilities.....</b>	<b>\$ 4,835</b>	<b>\$ 7,295</b>

### **Note 4 Other Income**

#### ***Grant income***

As of September 30, 2024, the Company had received a \$1.0 million research grant awarded 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 (blarcamesine) related to Parkinson’s disease. Of the total, \$0.5 million was received during the year ended September 30, 2023 and \$0.5 million was received during the year ended September 30, 2021.

The grant income has been deferred when received and is being amortized to other income as the related research and development expenditures are incurred. During the year ended September 30, 2024, the Company recognized \$75,000 (2023: \$25,000) of this grant on its statements of operations within grant income. At September 30, 2024 an amount of \$0.8 million (2023: \$0.9 million) of this grant is recorded as deferred grant income, representing the amount of this grant which has not yet been amortized to other income. The Company will recognize this income on its statements of operations as the related expenditures are incurred to offset the income.

#### ***Research and development incentive income***

Research and development incentive income represents the income earned by Anavex Australia of the Australia R&D credit. This cash incentive is received by Anavex Australia, upon filing of a claim in connection with Anavex Australia’s annual income tax return.



During the year ended September 30, 2024, the Company recorded research and development incentive income of \$2.3 million (AUD 3.5 million) (2023: \$2.7 million (AUD 4.1 million)) in respect of the Australia R&D credit for eligible research and development expenses incurred during the year. This amount is included within Other income (expense) on the consolidated statements of operations and comprehensive loss.

At September 30, 2024, Incentive and tax receivables includes \$2.3 million (AUD 3.3 million) (2023: \$2.5 million (AUD 3.9 million)) relating to Australia R&D credits earned during the year that are expected to be reimbursed upon filing of the Company's annual claim under this program.

The Australia R&D credit program is a self-assess program whereby the Company must assess its eligibility each year to determine (i) if the entity is eligible (ii) if the specific R&D activities are eligible and (iii) if the individual R&D expenditures have nexus to such R&D activities. 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. Anavex Australia is able to continue to claim the R&D tax incentive for as long as it remains eligible and continues to incur eligible research and development expenditures.

Although the Company believes that it has complied with all the relevant conditions of eligibility under the program for all periods claimed, the ATO has the right to review the Company's qualifying programs and related expenditures for a period of four years. If such a review were to occur, the ATO may have different interpretations of certain eligibility requirements. If the ATO disagreed with the Company's assessments and any related subsequent appeals, it could require adjustment to and repayment of current or previous years' claims already received. Additionally, if the Company was unable to demonstrate a reasonably arguable position taken on such claims, the ATO could also assess penalties and interest on any such adjustments.

Currently, the Company's tax incentive claims from 2020 to 2024 are open to potential review by the ATO. Additionally, the period open for review is indefinite if the ATO suspects fraud. The Company has not provided any allowance for any such potential adjustments, should they occur in the future.

## **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.

### ***2023 Purchase Agreement***

On February 3, 2023, the Company entered into a \$150.0 million purchase agreement (the "2023 Purchase Agreement") with Lincoln Park Capital Fund, LLC ("Lincoln Park"), pursuant to which the Company has the right to sell and issue to Lincoln Park, and Lincoln Park is obligated to purchase, up to \$150.0 million in value of its shares of common stock from time to time over a three-year period until February 3, 2026.

In consideration for entering into the 2023 Purchase Agreement, the Company issued to Lincoln Park 75,000 shares of common stock as a commitment fee (the "initial commitment shares") and agreed to issue up to an additional 75,000 shares pro rata, when and if, Lincoln Park purchased, at the Company's discretion, the \$150.0 million aggregate commitment. The Company determined the fair value of the initial commitment shares was \$0.8 million with reference to the closing price of the Company's shares on the Purchase Agreement date. In addition, the Company incurred third party expenses of \$0.1 million in connection with entering into the Purchase Agreement. These amounts were expensed to other financing expense on the statements of operations during the year ended September 30, 2023.

During the year ended September 30, 2024, the Company issued to Lincoln Park an aggregate of 2,455,646 shares of common stock under the 2023 Purchase Agreement, including 2,450,000 shares of common stock for an aggregate purchase price of \$11,283,200 and 5,646 commitment shares. During the year ended September 30, 2023, the Company issued to Lincoln Park an aggregate of 3,288,943 shares of common stock under the 2023 Purchase Agreement, including 3,275,000 shares of common stock for aggregate proceeds of \$27.9 million and 13,943 commitment shares.

At September 30, 2024, an amount of \$110.8 million remained available under the 2023 Purchase Agreement.

### ***2020 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 “2020 Sales Agreement”) with Cantor Fitzgerald & Co. and SVB Leerink LLC (together the “Sales Agents”), pursuant to which the Company could offer and sell shares of common stock registered under an effective registration statement from time to time through the Sales Agents (the “Offering”).

During the years ended September 30, 2024 and 2023, no shares were sold pursuant to the Offering. At September 30, 2023, an amount of \$142.4 million was registered pursuant to an effective registration statement.

On July 24, 2024, the Company terminated the 2020 Sales Agreement.

### **Note 6 Commitments and Contingencies**

#### ***Lease***

The Company leases office space under an operating lease with an initial term of 12 months or less. Under the terms of the office lease, the Company is required to pay its proportionate share of operating costs.

The operating lease costs were as follows (in thousands):

	<b>Years ended September 30,</b>	
	<b>2024</b>	<b>2023</b>
Operating lease costs.....	\$ 125	\$ 118

#### ***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.

The Company made matching contributions under the 401(k) plan as follows (in thousands):

	<b>Years ended September 30,</b>	
	<b>2024</b>	<b>2023</b>
Contributions to 401(k) plan.....	\$ 279	\$ 232

#### ***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.

On March 13, 2024, a shareholder class action complaint was filed in the United States District Court for the Southern District of New York and it named the Company and an officer of the Company as Defendants. The complaint was amended on July 12, 2024. The complaint alleges violations of the Securities and Exchange Act of 1934 associated with disclosures and statements made with respect to certain clinical trials for ANAVEX®2-73 related to Rett syndrome. The complaint seeks unspecified damages, as well as costs, including counsel and expert witness fees, on behalf of a class of investors. The Company believes the lawsuit is without merit and the Company denies any liability or wrongdoing and has filed motions to dismiss the complaints, which is awaiting a decision by the Court. No amount has been recorded in these consolidated financial statements for any loss contingencies associated with this lawsuit as the Company believes that it is not probable that any loss will occur.

On May 8, 2024, a similar complaint was filed in the same court by Kenneth Downing, a purported shareholder of the Company, against the same defendants. The Company believed that this lawsuit was also without merit and filed a motion to dismiss the complaint. Plaintiff Downing voluntarily dismissed this complaint subsequent to the filing of the motion to dismiss.

On or about May 13, 2024, a derivative lawsuit was filed against the Company (as nominal defendant), an officer of the Company, and members of the Company's Board of Directors in the U.S. District Court for the District of Nevada by another purported shareholder. The complaint asserts various common law claims (including breach of fiduciary duty) and violation of Section 14(a) of the Securities Exchange Act regarding the same or similar allegations at issue in the purported class action lawsuit related to disclosures and statements made about certain clinical trials related to Rett Syndrome. The Company believes this lawsuit is without merit and the Company denies any liability or wrongdoing. The parties are currently due to file a proposed schedule for the anticipated motion to dismiss by the Company and the officer of the Company (the other named defendants have not been served with the complaint) on or before January 15, 2025. No amount has been recorded in these consolidated financial statements for any loss contingencies associated with this lawsuit as the Company believes that it is not probable that any loss will occur.

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

### ***Share Purchase Warrants***

A summary of the status of the Company's outstanding share purchase warrants is presented below:

	Number of Warrants	Weighted Average Exercise Price (\$)
Balance, September 30, 2023.....	160,000	3.72
Expired.....	(150,000)	3.17
Balance, September 30, 2024.....	<u>10,000</u>	<u>12.00</u>

At September 30, 2024, the Company had 10,000 share purchase warrants outstanding exercisable at \$12.00 per share until April 21, 2026.

### ***Stock-based Compensation Plan***

#### ***2015 Stock Option Plan***

On September 18, 2015, the Company's Board 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 plan, in addition to the shares available under the 2019 Plan and the 2015 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, 2024, 5,267,500 options had been issued under the 2022 Plan and 5,462,202 options were available for issue under the 2022 Plan.

The following summarizes information about stock option activity during the years ended September 30, 2024 and 2023:

	Number of Options	Weighted Average Exercise Price (\$)	Weighted Average Grant Date Fair Value (\$)	Aggregate intrinsic value (\$)
Outstanding, October 1, 2022 .....	13,169,616	6.61	4.96	62,267,309
Granted.....	1,959,000	9.30	6.60	—
Exercised.....	(759,753)	2.34	0.95	4,629,026
Forfeited.....	(257,083)	12.00	6.74	—
Outstanding, September 30, 2023 .....	<u>14,111,780</u>	<u>7.12</u>	<u>5.27</u>	<u>22,290,069</u>
Granted.....	1,860,500	5.47	3.95	—
Exercised.....	(273,360)	2.53	1.11	601,407
Forfeited.....	(661,166)	11.67	5.00	—
Outstanding, September 30, 2024.....	<u>15,037,754</u>	<u>6.80</u>		<u>15,825,791</u>
Exercisable, September 30, 2024.....	<u>9,910,590</u>	<u>5.52</u>		<u>15,176,855</u>

The following summarizes information about stock options at September 30, 2024 by a range of exercise prices:

Range of exercises prices		Number of outstanding options	Weighted average remaining contractual life (in years)	Weighted average exercise price	Number of vested options	Weighted average exercise price
From	To					
\$ 0.92	\$ 3.00	3,015,700	3.79	\$ 2.39	3,015,700	\$ 2.39
\$ 3.01	\$ 5.00	2,267,500	4.01	\$ 3.42	2,056,250	\$ 3.31
\$ 5.01	\$ 9.00	6,640,554	6.07	\$ 6.58	3,473,639	\$ 6.21
\$ 9.01	\$ 13.00	1,649,000	7.33	\$ 10.26	760,000	\$ 10.50
\$ 13.01	\$ 25.00	1,465,000	6.45	\$ 18.18	605,001	\$ 18.47
		<u>15,037,754</u>	<u>5.48</u>	<u>\$ 6.80</u>	<u>9,910,590</u>	<u>\$ 5.52</u>

The weighted average per share fair value of options vested at September 30, 2024 was \$4.34 (2023: \$3.94). At September 30, 2024, the weighted average contractual life of options outstanding was 5.48 years (2023: 6.0 years) and for options exercisable was 4.03 years (2023: 4.75 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, 2024.

The Company recognized share-based compensation expense of \$9.4 million during the year ended September 30, 2024 (2023: \$16.4 million) in connection with the issuance and vesting of stock options 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 (in thousands):

	Years ended September 30,	
	2024	2023
General and administrative .....	\$ 3,625	\$ 5,558
Research and development .....	5,813	10,812
Total share-based compensation .....	<u>\$ 9,438</u>	<u>\$ 16,370</u>

An amount of approximately \$8.4 million in share-based compensation is expected to be recorded over the remaining term of such options and warrants through fiscal 2027.

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:

	2024	2023
Risk-free interest rate.....	4.28%	3.70%
Expected life of options (years) .....	5.78	5.64
Annualized volatility.....	84.81%	85.13%
Dividend rate.....	0.00%	0.00%

The fair value of stock compensation charges recognized during the years ended September 30, 2024 and 2023 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 (in thousands):

	<b>2024</b>	<b>2023</b>
United States .....	\$ (39,195)	\$ (41,198)
Foreign .....	(3,807)	(6,300)
Total .....	<u>\$ (43,002)</u>	<u>\$ (47,498)</u>

The components of net deferred income tax assets as of September 30, 2024 and 2023 are as follows (in thousands):

	<b>2024</b>	<b>2023</b>
Net operating loss carryforwards .....	\$ 48,134	\$ 46,462
Research and development tax credit carryforwards .....	4,203	2,713
Share-based compensation .....	21,091	18,593
Research and development capitalization .....	15,104	7,219
Unpaid charges .....	3,197	1,559
Intangible asset costs .....	758	593
Foreign exchange and other .....	(254)	49
Valuation allowance of deferred tax assets .....	(92,233)	(77,188)
Net deferred tax assets .....	<u>\$ —</u>	<u>\$ —</u>

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, 2024 and 2023 is as follows (in thousands):

	<b>2024</b>	<b>2023</b>
Income tax benefit at statutory federal rate .....	\$ (9,030)	\$ (9,975)
Foreign income taxed at other rates .....	(61)	—
Permanent differences relating to share-based compensation .....	(10)	(601)
Permanent differences relating to GILTI inclusion .....	—	165
Other permanent differences .....	(276)	273
Research and development credits, net .....	(860)	(37)
State and local taxes .....	(3,821)	(4,122)
Adjustment to true up to prior years' tax provision .....	(1,128)	206
Change in valuation allowances .....	15,186	14,098
Income tax expense .....	<u>\$ —</u>	<u>\$ 7</u>

As of September 30, 2024, the Company had U.S. federal net operating loss carryforwards of approximately \$128.5 million (2023: \$126.3 million) of which \$37.7 million will begin to expire in 2025 and \$90.8 million can be carried forward indefinitely, state and local net operating loss carryforwards of approximately \$ 16.9 million (2023: \$16.6 million) which will begin to expire in 2036, and Research and Development tax credits of approximately \$4.3 million (2023: \$2.7 million) which will begin to expire in 2029. The calculation of the Research and Development tax credits, by their nature, involve estimates and subjectivity. If examined by the U.S. federal and state tax authorities, it is possible that some portion of these credit carryforwards would be disputed by the tax authorities.

The Company had approximately \$16.6 million (approximately AU\$23.9 million) (2023: \$12.9 million (approximately AU\$20.1 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 valuation allowance has been established at September 30, 2024 and 2023.

The Tax Cuts and Jobs Act of 2017 (TCJA) has modified the IRC 174 expenses related to research and development for tax years beginning after December 31, 2021. Under the TCJA, the Company must now capitalize the expenditures related to research and development activities and amortize over five years for U.S. activities and 15 years for non-U.S. activities using a mid-year convention. Therefore, the capitalization of research and development costs in accordance with IRC 174 has resulted in a gross deferred tax assets at September 30, 2024 of \$15.1 million (2023: \$7.2 million).

#### Uncertain Tax Positions

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 2005.

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. 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, 2024 and 2023 the Company determined that there were no changes in ownership pursuant to Section 382.

As of September 30, 2024, 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.

#### Note 8 Subsequent Events

The Company evaluates subsequent events occurring between the most recent balance sheet date and the date the financial statements are available to be issued in order to determine whether the subsequent events are to be recorded and/or disclosed in the Company's financial statements and footnotes. The financial statements are considered to be available to be issued at the time they are filed with the Securities and Exchange Commission (SEC).

There were no subsequent events or transactions that required recognition or disclosure in the consolidated financial statements.

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## **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, 2024.

#### ***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, 2024.

#### ***Changes in Internal Control over Financial Reporting***

During the quarter ended September 30, 2024, there were no material 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 of our directors or Section 16 officers adopted, modified or terminated a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement" (in each case, as defined in Item 408(a) of Regulation S-K) during the three-month period ended September 30, 2024.

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

Not applicable.

## **PART III**

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

#### ***Directors and Executive Officers***

Our directors are to be elected at our annual meeting and each director elected is to hold office until his or her successor is elected and qualified. Our Board of Directors may remove our officers at any time.

Our directors and executive officers, their ages, positions held, and duration of such, are as follows:

<b>Name</b>	<b>Position</b>	<b>Age</b>	<b>Date first appointed</b>
Christopher Missling, PhD	Director, President, Chief Executive Officer, Secretary	59	July 5, 2013
Jiong Ma, PhD	Director, Chair	60	May 25, 2021
Athanasios Skarpelos	Director	58	January 9, 2013
Claus van der Velden, PhD	Director	52	March 2, 2018
Steffen Thomas, PhD	Director	59	June 15, 2015
Peter Donhauser, D.O.	Director	59	February 8, 2017
Sandra Boenisch, CPA, CGA	Principal Financial Officer, Treasurer	43	October 1, 2015

### ***Board Leadership Structure***

The Board of Directors is composed of a majority of independent directors and the Chief Executive Officer of the Company.

Our Board of Directors has appointed an independent Board Chair, Dr. Jiong Ma. As Board Chair, Dr. Ma has the authority, among other things, to call and preside over meetings of our Board, to set meeting agendas, and to determine materials to be distributed to the Board. The Company believes separation of the positions of Board Chair and Chief Executive Officer reinforces the independence of our Board in its oversight of the business and affairs of the Company. In addition, the Company believes that having an independent Board Chair creates an environment that is more conducive to objective evaluation and oversight of management's performance, increasing management accountability and improving the ability of our Board to monitor whether management's actions are in the best interests of the Company and its stockholders.

The Audit Committee, Compensation Committee, and Nominating and Corporate Governance Committee each have oversight over specific areas of responsibility, as discussed further below.

### ***Board of Directors' Role in Risk Oversight***

The Board of Directors is responsible for oversight of the Company's risk management process. The Board administers this oversight function directly through the Board of Directors as a whole, as well as through the committees of the Board. Areas of focus include economic risk, operational risk, financial risk (accounting, investment or liquidity, and tax), competitive risk, legal and regulatory risk, cybersecurity risk and compliance and reputational risks. The Board of Directors is supported by regular reporting by management, which is designed to give the Board of Directors visibility over the Company's operations and activities to adequately identify key risks and understand management's risk mitigation strategies.

### ***Business Experience***

The following is a brief account of the education and business experience of directors and executive officers during at least the past five years, indicating their principal occupations during the period, and the names and principal businesses of the organizations by which they were employed.

Christopher Missling, PhD. Christopher Missling has over twenty years of healthcare industry experience in big pharmaceutical, biotech and investment banking. Most recently, from March 2007 until his appointment by our Company, Dr. Missling served as the head of healthcare investment banking at Brimberg & Co. in New York, New York. In addition, Dr. Missling served as the Chief Financial Officer of Curis, Inc. (NASDAQ: CRIS) and ImmunoGen, Inc. (NASDAQ: IMGN). Dr. Missling earned his MS and PhD from the University of Munich and an MBA from Northwestern University Kellogg School of Management and WHU Otto Beisheim School of Management.

Jiong Ma, PhD. Jiong Ma has over 25 years of experience in investing, building, and scaling of companies with a focus on innovative product launches in digital health, technology and the new energy transition. Dr. Ma is a General Partner of Phoenix Venture Partners. She serves as Lead Independent Board Director of SES AI Corporation (NYSE: SES), Chairs the Compensation Committee, and as a member of Audit, Nominating, and Strategic Investment Committee. Dr. Ma served as senior partner and a member of the investment committee at Braemar Energy Ventures ("Braemar"). While at Braemar, Dr. Ma led investments in more than 15 companies involved in either resource efficiency, e-mobility, industrial digitalization, renewable energy, or deep tech, and has achieved multiple successful exits through M&A and IPO. Dr. Ma has significant knowledge and expertise in the technology industry, including information security. Prior to Braemar Energy Ventures, she was with the Venture Capital Group at 3i Group, a global private equity firm, where she led investments across multiple stages in Digital Health, TMT and Cleantech. Preceding the Venture Capital Group at 3i, Dr. Ma held several senior positions at Lucent Technologies and Bell Labs. Her responsibilities included lead roles in product portfolio



strategy, new product launches for Optical and Data Networking, and research and product development. Dr. Ma was also a founding team member of Onetta Inc., a fiber networks company. She has a PhD in Electrical and Computer Engineering from the University Colorado Boulder and an MS in Electrical Engineering from Worcester Polytechnic Institute. Dr. Ma is a Kauffman Fellow.

Claus van der Velden, PhD. Claus van der Velden, PhD brings significant expertise in management, accounting, internal controls, information security and risk management. Since May 2021, he has served as Managing Director (Chief Financial Officer) of NetCologne GmbH, a regional telecommunication provider in Germany. From July 2011 to May 2021, he served as corporate head of Management Accounting, Internal Audit and Risk Management at Stroeer SE & Co KGaA, a publicly listed German digital media company. As the prior head of internal audit at Stroeer SE & Co KGaA, Dr. van der Velden has experience in the area of information security risk assessment, and the internal control tools, processes, and policies needed to counter information security threats. Previously, Dr. van der Velden served as the Director of Corporate Business Controlling for the Nutrition & Health business unit at Cognis, a worldwide supplier of global nutritional ingredients and specialty chemicals. In this position, he was also a compliance representative and a member of the global leadership team. After the acquisition of Cognis by BASF, he was responsible for the management accounting processes of the BASF Nutrition & Health division, developing and producing mostly natural-source ingredients for the food and healthcare industries. Dr. van der Velden started his career as a strategy consultant at an international marketing and strategy consultancy firm. He studied in Kiel and Stockholm and received a degree in economics from the University of Kiel and later obtained his doctorate in business management from the WHU-Otto Beisheim School of Management where he also previously taught economics.

Athanasios Skarpelos. Athanasios (Tom) Skarpelos is a self-employed investor with over 20 years of experience working with private and public companies with a focus on biotechnology companies involved in drug discovery and drug development projects. His experience has led to relationships with researchers at academic institutes in Europe and North America. Mr. Skarpelos is a founder of Anavex.

Steffen Thomas, PhD. Steffen Thomas has over 15 years of experience as a European patent attorney and is currently practicing at Epping Hermann Fischer, a major intellectual property law firm in Europe. Previously, he worked for Japan-based Takeda Pharmaceutical Company, the largest pharmaceutical company in Asia and a top firm worldwide, as an in-house patent attorney. Prior to that, he worked for Nycomed Pharma, acquired by Takeda in 2011 for approximately USD \$10 billion. Dr. Thomas' legal practice covers drafting of patent applications, prosecuting patent applications before national and international patent offices, defending and challenging patents in opposition, appeal, and nullity proceedings, enforcing patents before the infringement courts, and preparing opinions on patentability and infringement in the technical field of chemistry. Dr. Thomas has particular expertise in small molecule pharmaceuticals. He holds MS and PhD degrees in Chemistry from the University of Munich.

Peter Donhauser, D.O. Peter Donhauser had more than 20 years of expertise in clinical research prior to practicing osteopathic medicine with an integrated medical approach in private practice beginning in 2000. He worked at the University Hospital of Munich in the fields of geriatrics and neuromusculoskeletal diseases. During this time, he was a clinical trial investigator in multiple Phase 3 studies, including studies sponsored by Merck Sharp & Dohme, Merck, Boehringer Mannheim, Roche, Servier and Sanofi. He received his human medicine degree at the University of Munich and Doctor of Osteopathic Medicine (D.O.) from the German-American Academy for Osteopathy, or DAAO, a member of the European Register for Osteopathic Physicians, or EROP, at the Philadelphia College of Osteopathic Medicine.

Sandra Boenisch, CPA, CGA. Ms. Boenisch is a Chartered Professional Accountant (CPA, CGA) with approximately 20 years of accounting, audit and financial reporting experience in a variety of industries, both in the United States and Canada. Ms. Boenisch was an independent consultant, providing financial reporting services to a range of public companies in the United States and Canada since January 2012. From 2008 until 2012, Ms. Boenisch was employed at BDO Canada LLP (Vancouver, BC) where she was hired as a Senior Accountant and was later promoted to Manager, Audit Assurance. Ms. Boenisch specialized in managing assurance engagements for public companies in the United States and Canada. Prior to that, Ms. Boenisch worked for another public accounting firm from 2001 to 2008. As an independent consultant, Ms. Boenisch has acquired considerable experience in finance, governance, and regulatory compliance. She holds a BComm from Laurentian University.

### ***Family Relationships***

There are no family relationships between any director or executive officer.

### ***Involvement in Certain Legal Proceedings***

There are no material proceedings to which any director or executive officer or any associate of any such director or officer is a party adverse to our Company or has a material interest adverse to our Company.

### ***Delinquent Section 16(a) Reports***

Section 16(a) of the Exchange Act requires our officers and directors, and persons who beneficially own more than ten percent (10%) of our outstanding common stock, to file initial reports of ownership and reports of changes in ownership with the SEC. Such persons are required by SEC regulations to furnish us with all copies of Section 16(a) forms they file.

Based solely on our review of the forms furnished to us and written representations from certain reporting persons, we believe that all filing requirements applicable to our executive officers, directors and persons who own more than 10% of our common stock were complied with in fiscal year 2024, except for the following late filings:

- Form 4 filed January 12, 2024 for Sandra Boenisch;
- Form 4 filed January 12, 2024 for Christopher Missling;
- Form 4 filed February 23, 2024 for Athanasios Skarpelos;
- Form 4 filed February 23, 2024 for Jiong Ma;
- Form 4 filed February 23, 2024 for Steffen Thomas;
- Form 4 filed February 23, 2024 for Peter Donhauser; and
- Form 4 filed February 23, 2024 for Claus van der Velden.

### ***Business Code of Conduct & Ethics***

Our Board adopted a code of business ethics and conduct (the “Code of Ethics”), applicable to all of our executives, directors and employees. The Code of Ethics is available in print to any stockholder that requests a copy. Copies may be obtained by contacting Investor Relations at our corporate headquarters. Our Code of Ethics is also available on our website at [www.anavex.com/corporate-governance](http://www.anavex.com/corporate-governance). We intend to make any disclosures regarding amendments to, or waivers from, the Code of Business Conduct required under Form 8-K by posting such information on our website.

### ***Insider Trading Policy***

We have an Insider Trading Policy that provides guidelines with respect to transactions in our securities by insiders and the handling of our confidential information and the confidential information of the companies with which we engage in transactions or do business. The policy promotes compliance with U.S. federal, securities laws that prohibit certain persons who are aware of material non-public information relating to us from (1) purchasing, selling, or otherwise engaging in transactions in our securities, or (2) providing material non-public information to other persons who may trade on the basis of that information. In addition, our Insider Trading Policy prohibits our directors, officers, employees and consultants from engaging in short sales, transactions in publicly traded options such as put, calls or other derivative securities, hedging transactions and other inherently speculative transactions with respect to our stock at any time. Our policy further prohibits such persons from engaging in transactions involving any loan, pledge or other transfer of beneficial ownership of the Company’s securities without obtaining advance clearance of the proposed transaction from our Insider Trading Compliance Officer.

### ***Information Regarding Committees of the Board of Directors***

The Board has an Audit Committee, a Compensation Committee and a Nominating and Corporate Governance Committee. The following table provides membership and meeting information for 2024:

Name	Audit Committee	Compensation Committee	Nominating and Corporate Governance Committee
Christopher Missling, PhD.....			
Jiong Ma, PhD .....	X		
Claus van der Velden, PhD .....	X*	X*	X*
Athanasios Skarpelos.....			

Name	Audit Committee	Compensation Committee	Nominating and Corporate Governance Committee
Steffen Thomas, PhD .....	X	X	X
Peter Donhauser, D.O. ....		X	X
Meetings in 2024.....	4	2	1

\*Committee Chair

### ***Audit Committee and Audit Committee Financial Experts***

The Audit Committee is composed of four directors, each of whom is independent. The Audit Committee operates under a charter that was adopted by our Board of Directors. The Audit Committee oversees and reports to our Board of Directors on various auditing and accounting-related matters, including, among other things, the maintenance of the integrity of our financial statements, reporting process and internal controls; the selection, evaluation, compensation and retention of our independent registered public accounting firm; legal and regulatory compliance, including our disclosure controls and procedures; and oversight over our risk management policies and procedures.

Our Board of Directors has determined that Claus van der Velden is an “audit committee financial expert” as defined by applicable SEC and NASDAQ rules.

The Audit Committee has reviewed and discussed the audited consolidated financial statements with management. The Audit Committee has discussed with the Company’s independent registered public accounting firm the matters required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board (“PCAOB”) and the Securities and Exchange Commission (the “SEC”). In addition, the Audit Committee has received the written disclosures and the letter from the independent registered public accounting firm required by applicable requirements of the PCAOB regarding the firm’s communications with the Audit Committee concerning independence and has discussed with the independent registered accounting firm its independence from the Company and management. Based on the reviews and discussions referred to above, the Audit Committee recommended to the Board that the audited consolidated financial statements for the Company for the fiscal year ended September 30, 2024 be included in this Annual Report on Form 10-K for the year ended September 30, 2024.

The foregoing report has been furnished by the Audit Committee.

Claus van der Velden (Chairman)  
Jiong Ma  
Steffen Thomas

### ***Compensation Committee***

The Compensation Committee is composed of three directors, each of whom is independent. The Compensation Committee operates under a charter that was adopted by our Board of Directors. The Compensation Committee assists our Board of Directors in discharging its responsibilities relating to the compensation of our directors and executive officers. Its responsibilities include, among other things: reviewing, approving and recommending compensation programs and arrangements applicable to our officers; determining the objectives of our executive officer compensation programs; overseeing the evaluation of our senior executives; administering our incentive compensation plans and equity-based plans, including reviewing and granting equity awards to our executive officers; and reviewing and approving director compensation and benefits. The Compensation Committee can delegate to other members of our Board of Directors, or an officer or officers of the Company, the authority to review and grant share-based compensation for employees who are not executive officers.

The Compensation Committee has the responsibilities and authority designated by NASDAQ rules and the Compensation Committee Charter. Specifically, the Compensation Committee has the sole discretion to select and receive advice from a compensation consultant, legal counsel or other adviser and is directly responsible for oversight of their work. The Compensation Committee must also determine reasonable compensation to be paid to such advisors by us.

The Compensation Committee met two times during fiscal 2024 and acted by written consent as required.

## ***Nominating and Corporate Governance Committee***

The Nominating and Corporate Governance Committee (the “NCG Committee”) is appointed by the Board to oversee and evaluate the Board’s performance and the Company’s compliance with corporate governance regulations, guidelines and principles, to identify individuals qualified to become Board members, to recommend to the Board proposed nominees for Board membership, and to recommend to the Board directors to serve on each standing committee. The NCG Committee seeks to assemble a Board that possesses the appropriate balance of professional and industry knowledge, financial expertise and management experience that is necessary to oversee the Company’s business. The NCG also recognizes the importance of diversity in board composition, including diversity of experience, gender and ethnicity and seeks to continually strive towards optimal diversity. The NCG Committee operates under a charter that was adopted by our Board of Directors.

The NCG Committee met one time during fiscal 2024 and also acted by written consent as required.

## **ITEM 11. EXECUTIVE COMPENSATION**

### **Our Executive Compensation Program and Philosophy**

The intent of the Company’s compensation program for our named executive officers is to attract and retain talent, to create incentives for and to reward excellent performance. We seek to compensate our named executive officers in a manner that is competitive, rewards performance that creates stockholder value, recognizes individual contributions, and encourages long-term value creation.

The Compensation Committee meets at least once per year to review and evaluate the compensation of our named executive officers and each officer’s performance. The Compensation Committee utilizes quantitative and qualitative factors, including the accomplishment of initiatives, attitude, and leadership and applies overall judgment to assess performance, taking into account the financial condition of the Company. In setting compensation, the Compensation Committee considers the outcome of the most recent say-on-pay vote, as well as stockholder feedback throughout the year, when making compensation decisions for our executive officers. In our most recent say-on-pay vote, conducted at our 2024 annual meeting of stockholders, held on June 18, 2024, our stockholders approved the compensation of our named executive officers on an advisory basis, with 83.8% of the votes cast in favor of the compensation of our named executive officers. Ultimately, the Compensation Committee seeks to evaluate, based on the achievement of financial and nonfinancial objectives, the variable compensation, including special awards, of our named executive officers and decide on the base salary and target discretionary bonus for such persons taking into account relevant benchmark data.

The Compensation Committee believes that a significant portion of each named executive officer’s compensation opportunity should be tied to variable compensation and value creation for stockholders. The Compensation Committee believes this mix provides an appropriate balance between the financial security required to attract and retain qualified individuals, and the Compensation Committee’s goal of ensuring that the compensation of our named executive officers rewards performance that benefits stockholders over the long term.

### **Compensation Consultants**

The Compensation Committee makes recommendations to the Board regarding the compensation of our named executive officers, including the structure and design of the compensation programs. The Compensation Committee is responsible for retaining and terminating compensation consultants and determining the terms and conditions of their engagement. During fiscal 2024, the Compensation Committee did not engage any compensation consultants.

### ***Annual Discretionary Cash Bonuses***

The Company has an annual discretionary cash bonus program. We provide such bonuses to motivate executive officers to perform on behalf of general corporate goals and to perform in their areas of responsibility. The Compensation Committee works with the Chief Executive Officer to evaluate the Company’s financial performance of the prior year, and overall financial condition of the Company to determine if discretionary bonuses are to be paid. In addition, on an annual basis, our Compensation Committee independently evaluates the performance of our Chief Executive Officer in the prior year, as well as the overall financial condition of the Company to determine if a discretionary bonus of up to 20% of base salary shall be paid to the Chief Executive Officer.

## **Clawback Policy**

In November 2023, the Board adopted an executive officer compensation clawback policy that may be applied in the event of a material financial restatement. The clawback policy covers all of the named executive officers and includes all incentive-based compensation. Specifically, in the event of an accounting restatement, the Company must recover, reasonably promptly, erroneously awarded compensation in amounts determined pursuant to the policy. Compensation that may be recoverable under the policy includes cash or equity-based compensation for which the grant, payment or vesting (or any portion thereof) is or was predicated upon the achievement of specified financial results that are impacted by the material financial restatement, and the amount of compensation that may be impacted by the clawback policy is the difference between the amount paid or granted, and the amount that should have been paid or granted, if calculated on the updated financials. Recovery under the policy with respect to an executive officer will not require the finding of any misconduct by such executive officer or such executive officer being found responsible for the accounting error leading to an accounting restatement. Our equity awards provide that the Company may annul an award if the grantee incurs a separation from service for “cause” (as defined in the agreements). In such case, all awards and any amounts or benefits received or outstanding shall be subject to cancellation, recoupment, rescission, payback and other action in accordance with the terms of the clawback policy or any applicable law. In addition, in the event of a restatement of the Company’s financial statements due to material noncompliance with any financial reporting requirement under the law, whether such noncompliance is the result of misconduct or other circumstances, an employee shall be required to reimburse the Company for any amounts earned or payable with respect to an award granted under the Company’s equity plan to the extent required by law and the Company’s clawback policy.

## **Stock Ownership Guidelines**

We do not have any stock ownership guidelines, ownership goals or holding requirements. If and as we succeed in achieving approval for and commercializing our product candidates, we expect that we will adapt the elements of our compensation program as appropriate and may include or substitute other elements in our compensation program. Changes in the elements of our compensation program may also reflect changes in the importance of tax or accounting treatments of a particular element of our compensation program.

## **Policies and Practices for Granting Certain Equity Awards**

Our policies and practices regarding the granting of equity awards are carefully designed to ensure compliance with applicable securities laws and to maintain the integrity of our executive compensation program. The Compensation Committee is responsible for the timing and terms of equity awards to executives and other eligible employees.

The timing of equity award grants is determined with consideration to a variety of factors, including but not limited to, the achievement of pre-established performance targets, market conditions and internal milestones. The Company does not follow a predetermined schedule for the granting of equity awards; instead, each grant is considered on a case-by-case basis to align with the Company’s strategic objectives and to ensure the competitiveness of our compensation packages.

In determining the timing and terms of an equity award, the Board or the Compensation Committee may consider material nonpublic information to ensure that such grants are made in compliance with applicable laws and regulations. The Board’s or the Compensation Committee’s procedures to prevent the improper use of material nonpublic information in connection with the granting of equity awards include oversight by legal counsel and, where appropriate, delaying the grant of equity awards until the public disclosure of such material nonpublic information.

The Company is committed to maintaining transparency in its executive compensation practices and to making equity awards in a manner that is not influenced by the timing of the disclosure of material nonpublic information for the purpose of affecting the value of executive compensation. The Company regularly reviews its policies and practices related to equity awards to ensure they meet the evolving standards of corporate governance and continue to serve the best interests of the Company and its shareholders.

## ***Summary Compensation***

The particulars of compensation paid to our named executive officers for the last three completed fiscal years:



<b>Name and Principal Position</b>	<b>Year</b>	<b>Salary (\$)</b>	<b>Bonus (\$)</b>	<b>Option Awards (\$)</b>	<b>All other Compensation (\$)<sup>(1)</sup></b>	<b>Total (\$)</b>
Christopher Missling, PhD.....	2024	700,000	140,000	1,927,600	16,100	2,783,700
President, Chief Executive Officer, and Director .....	2023	700,000	124,753	3,066,200	3,500	3,894,453
	2022	586,400	110,000	6,045,043	12,200	6,753,643
Sandra Boenisch <sup>(2)</sup> .....	2024	201,468	—	192,700	8,059	402,227
Principal Financial Officer and .....	2023	186,883	—	306,700	7,475	501,058
Treasurer .....	2022	174,900	—	277,603	—	452,503

(1) Comprised of employer matching of defined contribution savings plans.

(2) Compensation to Ms. Boenisch denominated in Canadian Dollars and has been translated to US dollars at an exchange rate of 0.73733 during the year ended September 30, 2024 (2023: 0.7416; 2022: 0.7831).

### ***Employment Agreements***

#### **Christopher Missling**

We and Dr. Missling entered into an employment agreement dated July 5, 2013, as amended and extended most recently by the third amendment effective April 7, 2022 (the “CEO Employment Agreement”), whereby we currently pay Dr. Missling an annual base salary of \$700,000. In addition, Dr. Missling is eligible to earn an annual cash bonus for each whole or partial calendar year of up to twenty percent of his base salary, and to participate in our employee benefit plans. We have agreed to indemnify Dr. Missling in connection with his provision of services to us.

#### **Sandra Boenisch**

We and Ms. Boenisch entered into an amended and restated employment agreement dated October 4, 2017, as amended and extended, whereby we currently pay Ms. Boenisch an annual base salary of \$279,840 Canadian dollars. Ms. Boenisch is eligible for discretionary salary increases.

### ***Outstanding Equity Awards at Fiscal Year-End***

The following table sets forth for each named executive officer and director certain information concerning the outstanding equity awards as of September 30, 2024.

<b>Name</b>	<b>Option Awards</b>			<b>Option Exercise Price (\$)</b>	<b>Option Expiration Date</b>
	<b>Number of Securities Underlying Exercisable Options (#)</b>	<b>Number of Securities Underlying Unexercisable Options (#)</b>	<b>Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)</b>		
Christopher.....	500,000	—	—	0.92	April 2, 2025
Missling.....	187,500	—	—	5.04	Sept 18, 2025
	379,625	—	—	6.26	July 5, 2026
	861,429	—	—	7.06	July 18, 2026
	500,000	—	—	3.28	Sept 22, 2026
	450,000	—	—	5.92	May 12, 2027
	400,000	—	—	3.30	Dec 13, 2027
	450,000	—	—	2.30	May 15, 2028
	409,500	—	—	2.58	Oct. 1, 2028

Option Awards					
Equity Incentive Plan Awards:					
Name	Number of Securities Underlying Exercisable Options (#)	Number of Securities Underlying Unexercisable Options (#)	Number of Securities Underlying Unexercised Unearned Options (#)	Option Exercise Price (\$)	Option Expiration Date
	750,000	—	—	3.15	May 3, 2029
	550,000	—	—	2.96	January 6, 2030
	550,000	—	—	5.49	December 30, 2030
	—	500,000	—	18.11	August 2, 2031
	—	500,000	—	7.54	June 14, 2032
	125,000	375,000	—	10.09	June 27, 2032
	—	500,000	—	8.57	March 31, 2033
	—	500,000	—	5.36	February 20, 2034
Sandra Boenisch.....	30,000	—	—	3.30	Dec 13, 2027
	30,000	—	—	2.30	May 15, 2028
	27,300	—	—	2.58	Oct. 1, 2028
	35,000	—	—	2.93	June 4, 2029
	70,000	—	—	2.96	January 6, 2030
	50,000	—	—	5.49	December 30, 2030
	—	40,000	—	18.11	August 2, 2031
	10,000	30,000	—	10.09	June 27, 2032
	—	50,000	—	8.57	March 31, 2033
	—	50,000	—	5.36	February 20, 2034

On February 20, 2024, our Compensation Committee granted options to our Chief Executive Officer and Principal Financial Officer, which vest in four equal tranches based on four performance milestones including accomplishing (i) Regulatory submission of AD-004 for Alzheimer's disease (US or EU), (ii) Publication of a Fragile X preclinical study (iii) Initiation of new clinical study not yet announced and (iv) Readout of ANAVEX3-71 Phase 2 clinical trial in Schizophrenia.

### Compensation of Directors

The table below shows the compensation of our directors who were not our named executive officers for the fiscal year ended September 30, 2024:

Name	Fees Earned or Paid in Cash (\$)	Stock Awards (\$)	Option Awards (\$) <sup>(1)</sup>	Non-Equity Incentive Plan Compensation (\$)	Nonqualified Deferred Compensation Earnings (\$)	All Other Compensation (\$)	Total (\$)
Jiong Ma.....	41,000	—	202,200	—	—	—	243,200
Claus van der Velden.....	41,000	—	202,200	—	—	—	243,200
Athanasios Skarpelos.....	25,000	—	202,200	—	—	—	227,200
Steffen Thomas .....	25,000	—	202,200	—	—	—	227,200
Peter Donhauser.....	25,000	—	202,200	—	—	—	227,200

- (1) Includes stock option awards valued based on the aggregate grant date fair value of the award computed in accordance with FASB ASC Topic 718. The amounts shown in the table above do not necessarily reflect the actual value that may be realized by the non-employee director upon vesting. On September 30, 2024, the aggregate number of outstanding vested and unvested stock option awards held by each director was as follows: Dr. Ma possessed options to purchase 210,000 shares, Dr. van der Velden possessed options to purchase 355,500 shares, Mr. Skarpelos possessed options to purchase 405,500 shares, Dr. Thomas possessed options to purchase 455,500 shares and Dr. Donhauser possessed options to purchase 355,500 shares.

We currently compensate non-employee directors \$25,000 per year, paid quarterly. We compensate Dr. Ma an additional \$4,000 per quarter for acting as Chair. We compensate Claus van der Velden an additional \$4,000 per quarter for performing the functions of Chairman of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee.

We regularly grant members of the Board of Directors awards of options. Each Board member is granted options initially when they join the Board of Directors, which typically vest over a three-year period. Additionally, we grant awards on an annual basis. Annual awards of options typically vest in full on the first anniversary of grant date. In 2024, the annual grant was 50,000 options to each director.

In addition, directors are entitled to reimbursement for reasonable travel and other out-of-pocket expenses incurred in connection with attendance at meetings of our Board of Directors. Our Board of Directors may award further special remuneration to any director undertaking any special services on our behalf other than services ordinarily required of a director.

### ***Retirement or Similar Benefit Plans***

There are no arrangements or plans in which we provide retirement or similar benefits for our directors or executive officers.

### ***Resignation, Retirement, Other Termination, or Change in Control Arrangements***

#### **Potential Payments Upon Termination**

The Company is a party to employment contracts with our Chief Executive Officer and Principal Financial Officer that contain provisions for payment of severance upon termination by either the Company without cause or by the employee for good reason. General terms of these arrangements are described below.

Our CEO Employment Agreement with Dr. Missling contains provisions regarding our obligations upon his termination and upon a Change in Control. Any capitalized term not defined herein is used as defined in the CEO Employment Agreement. If Dr. Missling's employment is terminated by us without Cause, he is entitled to receive payments by us consisting of (i) reimbursement of any unpaid business expenses to which he is entitled to reimbursement that were incurred prior to the effective date of his termination, (ii) all vested compensation and benefits to which he is entitled as of the Termination Date, (iii) a severance payment consisting of the three times the sum of (a) his annual salary in effect at the time of termination and (b) the average of the annual Bonuses payable to him for the last three completed calendar years prior to the Termination Date, (iv) all outstanding and unvested stock options and all options previously vested will become and remain exercisable for no less than three years from the Termination Date; (v) all of his unvested and outstanding restricted stock, restricted stock units or other equity awards that are unvested and outstanding as of the Termination Date shall vest and be settled within ten business days after the Termination Date, (vi) life insurance coverage until the end of the term of the CEO Employment Agreement; and (vii) continued participation in all medical, dental and hospitalization benefits plans or programs for Dr. Missling and his eligible dependents for 36 months or until he receives similar benefits at a new employer, at his sole cost. If Dr. Missling's employment is terminated by him for Good Reason, he is entitled to receive the same as the above, however the severance payment will consist of three times his annual salary in effect at the time of termination and two times the average annual Bonuses payable to him for the last three completed calendar years prior to the Termination Date.

If Dr. Missling was terminated by the Company without cause on September 30, 2024, he would have been entitled to a severance payment of \$2.5 million. If Dr. Missling terminated his employment for Good Reason on September 30, 2024, he would have been entitled to a severance payment of \$2.3 million.

Our CFO Employment Agreement with Ms. Boenisch contains provisions regarding our obligations upon her termination. Any capitalized term not defined herein is used as defined in the CFO Employment Agreement. Under the CFO Employment Agreement, if Ms. Boenisch is terminated without Cause, the Company shall pay Ms. Boenisch severance compensation equal to six months base salary payable by the Company for the six-month period following the Termination. In addition, the Company must provide Ms. Boenisch thirty (30) day notice of her Termination. If the Company opts to have Ms. Boenisch cease providing services to the Company prior to the expiration of the thirty (30) day notice-period (the "Notice Period"), Ms. Boenisch shall receive the Compensation and Benefits for the full length of the Notice Period as if such period was not waived. In addition, any unvested stock options or stock awards vesting in the contract year of Termination held by Ms. Boenisch as of the Date of Termination shall immediately vest.

If Ms. Boenisch was terminated by the Company without cause on September 30, 2024, she would have been entitled to continued salary payments equal to \$0.1 million in total.

The following table presents accelerated vesting for certain equity awards outstanding at the time of the executive's termination for each Named Executive Officer, if employment were terminated by either the Company without cause or by Dr. Missling for good reason on September 30, 2024:

Named Executive Officer	Vesting Upon Termination	
	Unvested Stock Options (#)	Stock Option Awards Estimated Benefit (\$) <sup>(1)</sup>
Dr. Christopher Missling.....	2,375,000	160,000
Sandra Boenisch.....	— <sup>(2)</sup>	—

(1) Estimated benefit based on the closing stock price of \$5.68 at September 30, 2024.

(2) Ms. Boenisch's unvested stock options at September 30, 2024 all contained performance based vesting conditions, therefore such options would not automatically vest upon Termination.

### Potential Payments Upon Change in Control

If the Company is subject to a Change in Control, then the CEO Employment Agreement and the CFO Employment Agreement provide that all previously granted but unvested stock options held by Dr. Missling and Ms. Boenisch shall vest.

The following table presents accelerated vesting for certain equity awards outstanding to the Named Executive Officer, if a change in control had occurred at September 30, 2024:

Named Executive Officer	Vesting Due to Change in Control	
	Unvested Stock Options (#)	Stock Option Awards Estimated Benefit (\$) <sup>(1)</sup>
Dr. Christopher Missling.....	2,375,000	160,000
Sandra Boenisch.....	170,000	16,000

(1) Estimated benefit based on the closing stock price of \$5.68 at September 30, 2024.

*For a complete description of these terms and conditions please refer to the CEO Employment Agreement and CFO Employment Agreement (and their amendments) filed as exhibits to this Annual Report on Form 10-K.*

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

The following table sets forth, as of December 23, 2024, certain information with respect to the beneficial ownership of our common stock by each stockholder known by us to be the beneficial owner of more than 5% of our common stock and by each of our current directors and our named executive officers and by our current directors and executive officers as a group. We have determined the number and percentage of shares beneficially owned by such person in accordance with Rule 13d-3 under the Securities Exchange Act of 1934. This information does not necessarily indicate beneficial ownership for any other purpose.

Title of class	Name and address of beneficial owner	Amount and nature of beneficial ownership	Percent of class <sup>(1)</sup>
<b>Directors and Named Executive Officers</b>			
Common Stock	Christopher Missling (CEO/Director)	7,363,264 <sup>(2)</sup>	8.1%
Common Stock	Jiong Ma (Director, Chair)	110,000 <sup>(3)</sup>	*
Common Stock	Claus van der Velden (Director)	255,500 <sup>(4)</sup>	*
Common Stock	Athanasios Skarpelos (Director)	1,611,958 <sup>(5)</sup>	1.9%
Common Stock	Steffen Thomas (Director)	360,500 <sup>(6)</sup>	*
Common Stock	Peter Donhauser (Director)	260,500 <sup>(7)</sup>	*
Common Stock	Sandra Boenisch (Principal Financial Officer)	275,262 <sup>(8)</sup>	*

Title of class	Name and address of beneficial owner	Amount and nature of beneficial ownership	Percent of class <sup>(1)</sup>
<b>Common Stock 5% Holders</b>	<b>Directors &amp; Executive Officers as a group (7 persons)</b>	<b>10,236,984</b>	<b>11.1%</b>
Common Stock	The Vanguard Group 100 Vanguard Blvd Malvern, PA 19355	4,360,648 <sup>(9)</sup>	5.1%
Common Stock	BlackRock, Inc. 55 East 52 <sup>nd</sup> Street New York, NY 10055	6,671,075 <sup>(10)</sup>	7.9%

\*Less than 1%

- (1) Percentage of ownership is based on 84,815,517 of our common stock issued and outstanding as of December 23, 2024. Except as otherwise indicated, we believe that the beneficial owners of the common stock listed above, based on information furnished by such owners, have sole investment and voting power with respect to such shares, subject to community property laws where applicable. Beneficial ownership is determined in accordance with the rules of the Commission and generally includes voting or investment power with respect to securities. Shares of common stock subject to options or warrants currently exercisable or exercisable within 60 days, are deemed outstanding for purposes of computing the percentage ownership of the person holding such option or warrants but are not deemed outstanding for purposes of computing the percentage ownership of any other person.
- (2) Includes options to purchase 500,000 shares of our common stock at \$0.92 per share, options to purchase 187,500 shares of our common stock at \$5.04 per share, options to purchase 379,625 shares of our common stock at \$6.26 per share, options to purchase 861,429 shares of our common stock at \$7.06 per share, options to purchase 500,000 shares of our common stock at \$3.28 per share, options to purchase 450,000 shares of our common stock at \$5.92 per share, options to purchase 400,000 shares of our common stock at \$3.30 per share, options to purchase 450,000 shares of our common stock at \$2.30 per share, options to purchase 409,500 shares of our common stock at \$2.58 per share, options to purchase 750,000 shares of our common stock at \$3.15 per share, options to purchase 550,000 shares of our common stock at \$2.96 per share, options to purchase 550,000 shares of our common stock at \$5.49 per share and options to purchase 125,000 shares of our common stock at \$10.09 per share that are vested or are vesting within 60 days. Excludes options to purchase 500,000 shares of our common stock at \$18.11 per share, options to purchase 500,000 shares of our common stock at \$7.54 per share, options to purchase 375,000 shares of our common stock at \$10.09 per share, options to purchase 500,000 shares at \$8.57 per share and options to purchase 500,000 shares of common stock at \$5.36 per share that do not vest within 60 days.
- (3) Includes options to purchase 35,000 shares of our common stock at \$13.01 per share, options to purchase 25,000 shares of our common stock at \$18.11 per share, options to purchase 33,333 shares of our common stock at \$10.09 per share and options to purchase 16,667 shares of our common stock at \$8.57 per share that have vested or are vesting within 60 days. Excludes options to purchase 16,667 shares of our common stock at \$10.09 per share, options to purchase 50,000 shares of our common stock at \$8.57 per share and options to purchase 50,000 shares of common stock at \$5.36 per share that do not vest within 60 days.
- (4) Includes options to purchase 50,000 shares of our common stock at \$2.60 per share, options to purchase 45,500 shares of our common stock at \$2.58 per share, options to purchase 50,000 shares of our common stock at \$2.96 per share, options to purchase 35,000 shares of our common stock at \$5.49 per share, options to purchase 25,000 shares of our common stock at \$18.11 per share, options to purchase 33,333 shares of our common stock at \$10.09 per share and options to purchase 16,667 shares of common stock at \$8.57 per share that have vested or are vesting within 60 days. Excludes options to purchase 16,667 shares of our common stock at \$10.09 per share, options to purchase 50,000 shares of our common stock at \$8.57 per share and options to purchase 50,000 shares of common stock at \$5.36 per share that do not vest within 60 days.
- (5) Includes options to purchase 100,000 shares of our common stock at \$3.28 per share, options to purchase 45,500 shares of our common stock at \$2.58 per share, options to purchase 50,000 shares of our common stock at \$2.96 per share, options to purchase 35,000 shares of our common stock at \$5.49 per share, options to purchase 25,000 shares of our common stock at \$18.11 per share, options to purchase 33,333 shares of our common stock at \$10.09 per share and options to purchase 16,667 shares of common stock at \$8.57 per share that have vested or are vesting within 60 days. Excludes options to purchase 16,667 shares of our common stock at \$10.09 per share, options to purchase 50,000 shares of our common stock at \$8.57 per share and options to purchase 50,000 shares of common stock at \$5.36 per share that do not vest within 60 days.
- (6) Includes options to purchase 50,000 shares of our common stock at \$1.76 per share, options to purchase 100,000 shares of our common stock at \$3.28 per share, options to purchase 45,500 shares of our common stock at \$2.58 per share, options to purchase 50,000 shares of our common stock at \$2.96 per share, options to purchase 35,000 shares of our common stock at \$5.49 per share, options to purchase 25,000 shares of our common stock at \$18.11 per share, options to purchase 33,333 shares of our common stock at \$10.09 per share and options to purchase 16,667 shares of common stock at \$8.57 per share that have vested or are vesting within 60 days. Excludes options to purchase 16,667 shares of our common stock at \$10.09 per share, options to purchase 50,000 shares of our common stock at \$8.57 per share and options to purchase 50,000 shares of common stock at \$5.36 per share that do not vest within 60 days.



- (7) Includes options to purchase 50,000 shares of our common stock at \$5.39 per share, options to purchase 45,500 shares of our common stock at \$2.58 per share, options to purchase 50,000 shares of our common stock at \$2.96 per share, options to purchase 35,000 shares of our common stock at \$5.49 per share, options to purchase 25,000 shares of our common stock at \$18.11 per share, options to purchase 33,333 shares of our common stock at \$10.09 per share and options to purchase 16,667 shares of common stock at \$8.57 per share that have vested or are vesting within 60 days. Excludes options to purchase 16,667 shares of our common stock at \$10.09 per share, options to purchase 50,000 shares of our common stock at \$8.57 per share and options to purchase 50,000 shares of common stock at \$5.36 per share that do not vest within 60 days.
- (8) Includes options to purchase 30,000 shares of our common stock at \$3.30 per share, options to purchase 30,000 shares of our common stock at \$2.30 per share, options to purchase 27,300 shares of our common stock at \$2.58 per share, options to purchase 35,000 shares of our common stock at \$2.93 per share, options to purchase 70,000 shares of our common stock at \$2.96 per share, options to purchase 50,000 shares of our common stock at \$5.49 per share and options to purchase 10,000 shares of common stock at \$10.09 per share that have vested or are vesting within 60 days. Excludes options to purchase 40,000 shares of our common stock at \$18.11 per share, options to purchase 30,000 shares of our common stock at \$10.09 per share, options to purchase 50,000 shares of our common stock at \$8.57 per share and options to purchase 50,000 shares of common stock at \$5.36 per share that do not vest within 60 days.
- (9) Based on Schedule 13G/A as filed with the SEC and dated on February 13, 2024
- (10) Based on Schedule 13G/A as filed with the SEC and dated on January 25, 2024

### ***Change in Control***

We are unaware of any contract or other arrangement, the operation of which may at a subsequent date result in a change of control of our Company.

### ***Securities Authorized for Issuance under Equity Compensation Plans or Individual Compensation Arrangements***

The following table summarizes certain information regarding our equity compensation plan or individual compensation arrangements at September 30, 2024:

#### **Equity Compensation Plan Information**

<b>Plan Category</b>	<b>Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)</b>	<b>Weighted-average exercise price of outstanding options, warrants and rights (b)</b>	<b>Number of securities remaining available for future issuances under equity compensation plans (excluding securities reflected in column (a)) (c)</b>
Equity compensation plans approved by security holders...	22,050,553	7.02	5,462,202
Equity compensation plans not approved by security holders.....	—	—	—
<b>Total.....</b>	<b>22,050,553</b>	<b>7.02</b>	<b>5,462,202</b>

### ***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 shares of Common Stock were made available for issuance under the 2022 Plan, in addition to the shares available under the 2019 Omnibus Incentive Plan (the “2019 Plan”) and the 2015 Omnibus Incentive Plan (the “2015 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.

The purpose of the 2022 Plan is to retain the services of valued key employees and consultants of our Company and such other persons, and to encourage such persons to acquire a greater proprietary interest in our Company, thereby strengthening their incentive to achieve the objectives of the shareholders of our Company. The purpose is also to serve as an aid and inducement in the hiring of new employees and to provide an equity incentive to consultants.

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

### *Transactions with related persons*

There have been no transactions, since October 1, 2022, or currently proposed transactions, in which we were or are to be a participant and the amount involved exceeds the lesser of \$120,000 or one percent of the average of the smaller reporting company's total assets at year end for the last two completed fiscal years, and in which any of the following persons had or will have a direct or indirect material interest.

- i. any director or executive officer of our Company;
- ii. any beneficial owner of shares carrying more than 5% of the voting rights attached to our outstanding shares of common stock; and
- iii. any member of the immediate family (including spouse, parents, children, siblings and in-laws) of any of the foregoing persons.

### *Compensation of Named Executive Officers and Directors*

For information regarding compensation of named executive officers and directors, please see "Item 11. Executive Compensation."

### *Director Independence*

Under the NASDAQ Stock Market Rules, the Board has a responsibility to make an affirmative determination that those members of its Board that serve as independent directors do not have any relationships with the Company and its businesses that would impair their independence. The Board has determined that that Christopher Missling, PhD is not independent, as that term is defined by NASDAQ 5605(a)(2), because Mr. Missling serves as our President, Chief Executive Officer, and Secretary.

The Board has determined that that Claus van der Velden, Athanasios Skarpelos, Steffen Thomas, Peter Donhauser and Jiong Ma are independent, as that term is defined by NASDAQ 5605(a)(2) and the applicable rules of the Commission.

## ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

### *Fees Paid to Our Independent Registered Public Accounting Firm*

The following table sets forth the aggregate fees billed or expected to be billed to our Company for professional services rendered by our independent registered public accounting firm, Grant Thornton, LLP for the fiscal years ended September 30, 2024 and 2023:

	<b>2024</b>	<b>2023</b>
Audit Fees .....	\$ 446,250	\$ 444,098
Audit Related Fees .....	—	—
Tax Fees .....	—	—
All Other Fees .....	—	—
Total Fees .....	\$ 446,250	\$ 444,098

**Audit Fees.** Consist of fees billed for professional services rendered for the audits of our financial statements, reviews of our interim financial statements included in quarterly reports, services performed in connection with regular filings with the Commission for the fiscal years ended September 30, 2024 and 2023 in connection with statutory and regulatory filings or engagements.

## ***Policy on Pre-Approval by Audit Committee of Services Performed by Independent Registered Public Accounting Firm***

Our Audit Committee pre-approves all services provided by our independent registered public accounting firm. All of the above services and fees were reviewed and approved by our Audit Committee.

Our Audit Committee has considered the nature and amount of fees billed or expected to be billed by Grant Thornton LLP and believes that the provision of services for activities unrelated to the audit was compatible with maintaining Grant Thornton LLP's independence.

### **PART IV**

#### **ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES**

<b>Exhibit Number</b>	<b>Description</b>
<b>(3)</b>	<b>Articles of Incorporation and Bylaws</b>
3.1	Articles of Incorporation, as amended (incorporated by reference to our Annual Report on Form 10-K for the year ended September 30, 2021 filed on November 24, 2021)
3.2	Amended and Restated Bylaws (incorporated by reference to our Current Report on Form 8-K filed on April 14, 2023)
<b>(4)</b>	<b>Instruments Defining the Rights of Security Holders</b>
4.1	Description of Registrant's Securities (incorporated by reference to our Annual Report on Form 10-K filed on November 28, 2022)
4.2	Registration Rights Agreement, dated February 3, 2023, by and between the Company and Lincoln Park Capital Fund, LLC (incorporated by reference to our Quarterly Report on Form 10-Q filed on February 7, 2023)
<b>(10)</b>	<b>Material Contracts</b>
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, Annex B, dated February 11, 2019, as filed on February 11, 2019)
10.3^	2022 Omnibus Incentive Plan (incorporated by reference to our Proxy Statement, dated April 11, 2022, Annex A, filed on April 11, 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 14, 2013)
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 Report on 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 with Sandra 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	Purchase Agreement dated February 3, 2023 by and between the Company and Lincoln Park Capital Fund, LLC (incorporated by reference to our Quarterly Report on Form 10-Q filed on February 7, 2023)
<b>(14)</b>	<b>Code of Ethics</b>
14.1	Code of Ethics Adopted on August 1, 2023 (incorporated by reference to our Annual Report on Form 10-K filed on November 27, 2023)
19.1*	Insider Trading Policy
<b>(21)</b>	<b>Subsidiaries</b>
21.1*	Subsidiaries of the Registrant
<b>(23)</b>	<b>Consent</b>

23.1*	Consent of Independent Registered Public Accounting Firm
<b>(31)</b>	<b>Section 302 Certifications</b>
31.1*	Section 302 Certification of Christopher Missling, PhD.
31.2*	Section 302 Certification of Sandra Boenisch
<b>(32)</b>	<b>Section 906 Certifications</b>
32.1**	Section 906 Certification of Christopher Missling, PhD and Sandra Boenisch
<b>(97)</b>	<b>Policy Relating to Recovery of Erroneously Awarded Compensation</b>
97.1	Anavex Life Sciences Corp. Compensation Clawback Policy (incorporated by reference to our Annual Report on Form 10-K filed on November 27, 2023)
<b>(101)</b>	<b>XBRL</b>
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.

\*\* The certification attached as Exhibit 32.1 that accompanies this Form 10-K is not deemed filed with the SEC and is not to be incorporated by reference into any filing of the Registrant under the Securities Act or the Exchange Act, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

^ 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: December 23, 2024**

**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.

<u>Signatures</u>	<u>Title(s)</u>	<u>Date</u>
<u>/s/ Christopher Missling, PhD</u> Christopher Missling, PhD	Chief Executive Officer (Principal Executive Officer) and Director	December 23, 2024
<u>/s/ Sandra Boenisch</u> Sandra Boenisch, CPA, CGA	Principal Financial Officer and Treasurer (Principal Accounting Officer)	December 23, 2024
<u>/s/ Jiong Ma, PhD</u> Jiong Ma, PhD	Director, Chair	December 23, 2024
<u>/s/ Claus van der Velden, PhD</u> Claus van der Velden, PhD	Director	December 23, 2024
<u>/s/ Athanasios Skarpelos</u> Athanasios Skarpelos	Director	December 23, 2024
<u>/s/ Steffen Thomas, PhD</u> Steffen Thomas, PhD	Director	December 23, 2024
<u>/s/ Peter Donhauser, D.O.</u> Peter Donhauser, D.O.	Director	December 23, 2024