Forward Looking Statement

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<td>ANAVEX Expanding Pipeline: Potential for Significant Value Creation Near and Long Term</td>
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* = Orphan Drug Designation by FDA
Overview

- **Four Key Clinical Trials Enrolling:** Two Phase 2 Rett Syndrome Trials, Phase 2b/3 Alzheimer’s Disease, Phase 2 Parkinson’s Disease Dementia with Several Readouts in 2020

- Rett syndrome* program Fast Track Designation and eligible for Pediatric Priority Review Voucher

- Pursuing Large Markets With High Unmet Need by Applying Precision Medicine

- Novel CNS Mechanism of Action Upstream of Neurodevelopment And Neurodegeneration

- Compelling first Human Patient Data

- Sufficient Cash To Achieve Key Milestones – Including non-dilutive Cash from Australian Government for Alzheimer’s Trial, and from Rettsyndrome.org for Rett Syndrome Trial

*FDA and EMA granted ANAVEX®2-73 Orphan Drug Designation (ODD) for Rett syndrome
Catalysts to Drive Value

The company expects to achieve key clinical milestones

- Full enrollment Phase 2 Parkinson’s disease dementia (PDD)
- FDA Fast Track designation for Rett syndrome program (RTT)
- Full enrollment U.S. Phase 2 Rett syndrome (RTT)
- Full enrollment AVATAR Phase 2 Rett syndrome (RTT)
- Topline data U.S. Phase 2 Rett syndrome (RTT)
- Topline data AVATAR Phase 2 Rett syndrome (RTT)
- Topline data Phase 2 Parkinson’s disease dementia (PDD) – MID 2020
- Initiate EXCELLENCE Phase 2/3 in pediatric Rett syndrome (RTT)
- Data publications in 2020
Clinical Trials – MoA and First Clinical Data:

- Rett Syndrome (RTT)
- Alzheimer’s Disease (AD)
Neural cells suffer functional loss in neurological disorders which causes cellular stress

Pathologies include:

- $\text{A}\beta$, Tau and ApoE fragmentation and dysfunction
- Proteinopathy
- Microglia activation, migration, and dysregulation
- Apoptosis feedback loops that lead to neuronal degradation
- Autophagy dysfunction
- Mitochondrial Dysfunction and Oxidative Stress that leads to further neuronal degradation
- Neurodegeneration that spreads through a cascade of stress responses

S1R activates neuroprotective signals that help neurons return to homeostasis
ANAVEX®2-73 Establishes Human Proof-of-Concept and SIGMAR1 Target Occupancy

2D [18F]FTC-146-PET imaging of ANAVEX®2-73: Dose-dependent ANAVEX®2-73 Target Engagement

ANAVEX®2-73 positive response in functional (ADCS-ADL*) outcome in Alzheimer’s disease patients correlate with SIGMAR1 mRNA levels

Source: Reyes S et al, AAIC 2018; H Hampel et al., AAIC 2018; *Alzheimer’s Disease Cooperative Study Activities of Daily Living 23-item scale (ADCS-ADL)
Sigma-1 receptor agonists have been shown to restore neuronal functions in neurodegenerative processes. ANAVEX® 2-73 enhances autophagy and alleviates Tau pathology in neurodegenerative disease models. Sigma-1 receptor agonists have a neuroprotective effect in neurodegenerative disease models.
Rett Syndrome (RTT)

- Non-inherited genetic postnatal disorder caused by mutations in the MECP2 gene
  - Occurs almost exclusively in girls
  - Leads to severe impairments, affecting nearly every aspect of the child’s life
  - Impairment includes ability to speak, walk, eat and even breathe easily
  - Hallmark of RTT is near constant repetitive hand movements while awake
  - Occurs worldwide in approximately one in every 10,000 to 15,000 live female births

What is Rett Syndrome?

Devastating neuro-developmental disease in girls with both movement impairment and cognitive impairment

Source: https://www.rettsyndrome.org/about-rett-syndrome
U.S. Rett Syndrome ANAVEX®2-73-RS-001 Trial (NCT03758924)

SUMMARY
- Phase 2, safety, tolerability, efficacy for 7 weeks, oral, liquid formulation, 5 mg daily (relatively low dose)
- Part A: Intensive PK, n=6, Completed
- Part B: Randomized, double-blind, placebo-controlled, n=15, ongoing
- Females > 18 years, classic RTT w/MECP2 mutation
- Evaluations at baseline (Week 0), Week 4 & Week 7 (End of Treatment)
- Good safety and tolerability: No serious adverse events, only three grade 1-2 adverse events

EFFICACY*
- Global severity RSBQ and CGI-I
- RSBQ = Rett Syndrome Behavior Questionnaire
- CGI-I = Clinical Global Impressions – Improvements
- Secondary: Behavior (ADAMS), Sleep (CSHQ), VAS (top caregiver concerns), Seizure diary
- Response Biomarker*: Glutamate, GABA; Genetic biomarker: DNA & RNA profiles

*Preliminary evaluation of efficacy: two-tailed, nonparametric tests (conservative)

RSBQ Total
- Baseline
- Week 7
- \(p = 0.027\)

RSBQ Hand Behaviors
- Baseline
- Week 7
- \(p = 0.042\)

RSBQ Breathing Problems
- Baseline
- Week 7
- \(p = 0.042\)

Sleep – CSHQ-Waking During the Night
- Baseline
- Week 7
- \(p = 0.042\)
Phase II to Phase III
Phase III to NDA/BLA

28% 46% 55% 76%

Without Biomarkers With Patient Selection Biomarkers

Patient Selection with Biomarker Increases Probability of Success

Precision Medicine

In patients with RTT, MeCP2 deficiency leads to *increased* levels of Glutamate, in comparison to healthy controls\(^1,2,3\), which results in excitatory-inhibitory imbalance and further synaptic dysfunction.

Loss of synaptic homeostasis can impair nerve cells (neurons) and their connections.

Glutamate as potential biomarker of microglia activation and synaptic dysfunction

Phase 2 PART A: Reported Improvements Correlate with Biomarkers

U.S. Rett Syndrome ANAVEX®2-73-RS-001 Trial (NCT03758924)

REPORT on PART A: INTENSIVE PK SUBCOHORT
- Plasma levels of the biomarker Glutamate decreased significantly (Week 0 vs. Week 7; 2-tailed Wilcoxon signed rank test, p = 0.046)
- Levels of Glutamate at Week 7 directly correlated with CGI-I scores at Week 7 (2-tailed Spearman’s rho = 0.837, p = 0.038)
- Greater decreases in Glutamate associated with greater improvement in these efficacy scores
- GABA changes demonstrated an inverse correlation of the magnitude of Glutamate changes (2-tailed Spearman’s rho = -0.829, p = 0.042)

Significant Correlations: RSBQ & CGI-I
- CGHI at Week 7 vs. RSBQ Total at Week 7: p = 0.003

Significant Correlations: Glutamate & CGI-I
- Glutamate at Week 7 vs. CGHI at Week 7: p = 0.038

Significant Correlations: Glutamate & Hand Behaviors
- % Change in Glutamate vs. RSBQ Hand Behaviors: p = 0.021

Significant Correlations: Glutamate & Sleep
- Glutamate μmol/L at Week 7 vs. Sleep CSHQ Total Visit 7: p = 0.005

Glutamate decreases by over 40%

Improvement
ANAVEX®2-73 Phase 2 U.S. Rett Syndrome Study

N=21*

RTT patient population

- Diagnosis of confirmed RTT
- Patients age >18
- DNA and RNA sequencing

Randomization 3:2

Primary and Secondary Endpoints
- PK, Safety and tolerability of ANAVEX®2-73
- Behavioral symptoms
- Sleep function
- Seizure activity

Pre-specified Endpoints
- Genetic variants SIGMAR1 (rs1800866), COMT (rs113895332/rs61143203) with influence on treatment effect

* Includes a 6 patient cohort undergoing a 7-week pharmacokinetic (PK) assessment with safety, tolerability, pharmacokinetic and efficacy evaluation of ANAVEX®2-73

* Oral liquid solution once daily; Dose restricted to maintain complete blinding
ANAVEX®2-73 Phase 2 Rett Syndrome AVATAR Study

N=33*

RTT patient population

- Diagnosis of confirmed RTT
- Patients age >18
- DNA and RNA sequencing

Randomization 3:2

ANAVEX®2-73 Active dose#

Placebo

Primary and Secondary Endpoints
- Safety and tolerability of ANAVEX®2-73
- Behavioral symptoms
- Sleep function
- Seizure activity

Pre-specified Endpoints
- Genetic variants SIGMAR1 (rs1800866), COMT (rs113895332/rs61143203) with influence on treatment effect

* Includes a 3 patient cohort undergoing a 3-week pharmacokinetic (PK) assessment with safety, tolerability, pharmacokinetic and efficacy evaluation of ANAVEX®2-73

* Oral liquid solution once daily; Dose restricted to maintain complete blinding
ANAVEX®2-73-RS-003 Rett Syndrome EXCELLENCE Study

N = 69

RTT patient population

- Diagnosis of confirmed RTT
- Patients age 5-18
- DNA and RNA sequencing

Primary and Secondary Endpoints
- Safety and tolerability of ANAVEX®2-73
- Behavioral symptoms
- Sleep function
- Seizure activity

Pre-specified Endpoints
- Genetic variants SIGMAR1 (rs1800866), COMT (rs113895332/rs61143203) with influence on treatment effect

Randomization 2:1

ANAVEX®2-73 Active dose#

Placebo

12 WEEK STUDY

* Oral liquid solution once daily; Dose restricted to maintain complete blinding
Alzheimer’s Disease (AD)

Alzheimer’s disease, progressive, irreversible neurological disease and most common cause of dementia

- Alzheimer’s disease incidence highly correlates with age
  - AD prevalence in US: ~5,700,000
  - Estimated 50 million people live with dementia worldwide
  - Today, there are no commercially available therapies to address the underlying cause of Alzheimer’s
  - The current annual cost of dementia is estimated at $1 trillion, a figure set to double by 2030

Source: www.alz.org/alzheimers-dementia/what-is-dementia/types-of-dementia/parkinsons-disease-dementia
ANAVEX®2-73 Demonstrated Improved MMSE\(^1\) and ADCS-ADL\(^2\) Scores in Phase 2a AD Study through 148 Weeks

Source: Hampel H., Afshar M., Parmentier F. et al., CTAD 2018; Hampel et al., Alzheimer's & Dement [accepted]

1 Mini Mental State Examination (MMSE)
2 Alzheimer’s Disease Cooperative Study Group - Activities of Daily Living Inventory (ADCS-ADL)
ANAVEX®2-73 Phase 2b/3 Alzheimer's Disease and ATTENTION-AD OLE Study

**N=450**

**Early AD patient population**
- Confirmed amyloid pathophysiology (CSF/amyloid PET)
- Patients aged 60 to 85 years
- MMSE score 20-28
- DNA and RNA sequencing

**Randomization 1:1:1**
- ANAVEX®2-73 High dose#
- ANAVEX®2-73 Medium dose#
- Placebo

**Primary Endpoints**
- ADAS-Cog
- ADCS-ADL
- Safety and tolerability of ANAVEX®2-73

**Key Secondary Endpoints**
- CDR-SB
- Structural and functional MRI
- Biomarkers: Abeta$_{40}$/Abeta$_{42}$, T-tau, P-tau, NFL, YKL-40, neurogranin, BACE1

**Pre-specified Endpoints**
- Genetic variants SIGMAR1 (rs1800866), COMT (rs113895332/rs61143203) with influence on treatment effect

**Oral capsule once daily; Dose restricted to maintain complete blinding**
Parkinson’s Disease Dementia (PDD)

- Parkinson’s disease is a fairly common neurological disorder in older adults, estimated to affect nearly 2 percent of those older than age 65
  - PD prevalence in US: ~1,000,000
  - The brain changes caused by Parkinson’s disease begin in a region that plays a key role in movement
  - As Parkinson’s brain changes gradually spread, they often begin to affect mental functions, including memory and the ability to pay attention, make sound judgments and plan the steps needed to complete a task

Source: www.alz.org/alzheimers-dementia/what-is-dementia/types-of-dementia/parkinson-s-disease-dementia
ANAVEX®2-73 Phase 2 Parkinson’s Disease Dementia (PDD) Study

N=120

PDD patient population

- Diagnosis of probable Parkinson’s disease dementia (PDD)
- Diagnosis of idiopathic Parkinson’s disease
- Patients aged ≥ 50 years
- MoCA score 13-23
- DNA and RNA sequencing

Randomization 1:1:1

ANA VEX®2-73 High dose#

ANA VEX®2-73 Medium dose#

Placebo

14 WEEK STUDY

Primary Endpoints
- CDR Continuity of Attention
- Safety and tolerability of ANAVEX®2-73

Key Secondary Endpoints
- MDS-UPDRS
- Sleep function
- Actigraphy
- MoCA
- Other CDR battery measures

Pre-specified Endpoints
- Genetic variants SIGMAR1 (rs1800866), COMT (rs113895332/ rs61143203) with influence on treatment effect

*Oral capsule once daily; Dose restricted to maintain complete blinding
Primary Endpoint ‘CDR Continuity of Attention’ of PDD ANAVEX®2-73 Ph2 Study: Confirmed Beneficial Effect in Previous Ph2a AD Study

Identification (IDN) in Cogstate battery assessed in ANAVEX®2-73 Ph2a AD Study comparable to CDR Continuity of Attention (choice reaction time paradigm)

Eli Lilly and Company uses ‘Continuity of Attention’ as Primary Endpoint in D1PAM’s dementia associated with Parkinson’s disease trial (ClinicalTrials.gov Identifier: NCT03305809)
ANAVEX®2-73 Ph2 AD Study - Cogstate IDN Improves within Weeks

Cogstate IDN from Baseline

[Graph showing data on Cogstate IDN improvements from baseline over weeks.]
Cogstate IDN: ANAVEX®2-73 Ph2a AD Patients Improve within Weeks vs Standard of Care AD Patients

AIBL-ROCS-AD* cohort as standard of care comparator

Anavex is the only Company pursuing Large Markets by Applying Precision Medicine to Develop Treatments for both Global Aging CNS diseases (Alzheimer’s, Parkinson’s), as well as catastrophic Orphan Genetically caused diseases, Rett Syndrome with High Unmet Needs

$ 277B
Economic burden
2018 Alzheimer’s Association

OVERARCHING MESSAGE
A novel approach is needed to address the totality of CNS diseases

PRECISION MEDICINE IMPROVES CHANCE OF CLINICAL SUCCESS
Testing for biomarkers demonstrated improved clinical response to ANAVEX®2-73 in Rett syndrome correlated with glutamate and for Alzheimer’s patients carrying wild-type (WT) SIGMAR1 and COMT genes

STRONG IP POSITION AROUND NOVEL MECHANISM OF ACTION
ANA VEX®2-73, is an orally available Sigma-1 receptor agonist that has been shown to restore homeostasis (composition of matter patent protection to 2037)

COMPELLING INITIAL HUMAN DATA
ANAVEX®2-73 undergoing Phase 2 in Rett syndrome and Phase 2a trial in Alzheimer’s disease with favorable safety and exploratory efficacy results through 148 weeks

VALUE-CREATING CATALYSTS
Clinical data readouts from two Phase 2 Rett syndrome studies and Phase 2 Parkinson’s disease dementia study anticipated in 2020. Clinical data publications and additional indications to be announced in 2020

SUFFICIENT CASH TO ACHIEVE KEY MILESTONES
Cash on hand and non-dilutive cash from Australian government for Alzheimer’s study, and from Rettsyndrome.org for Rett syndrome study
Anavex Life Sciences Expertise

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Walter E Kaufmann, MD - Chief Medical Officer
Stephan Toutain, MS, MBA – Chief Operating Officer
Emmanuel O Fadiran, RPh, PhD - SVP of Regulatory Affairs
Daniel Klamer, PhD - VP of Business Development & Scientific Strategy

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