
anavex®
LIFE SCIENCES Corp.
Corporate Presentation
Christopher U Missling, PhD | President & CEO
Nasdaq: AVXL | May 2022

Forward Looking Statement

This presentation contains forward-looking statements made within the meaning of the Private Securities Litigation Reform Act of 1995 by Anavex® Life Sciences Corp. and its representatives. These statements can be identified by introductory words such as “expects,” “plans,” “intends,” “believes,” “will,” “estimates,” “forecasts,” “projects,” or words of similar meaning, and by the fact that they do not relate strictly to historical or current facts. Forward-looking statements frequently are used in discussing potential product applications, potential collaborations, product development activities, clinical studies, regulatory submissions and approvals, and similar operating matters. Many factors may cause actual results to differ from forward-looking statements, including inaccurate assumptions and a broad variety of risks and uncertainties, some of which are known and others of which are not. Known risks and uncertainties include those identified from time to time in reports filed by Anavex Life Sciences Corp. with the Securities and Exchange Commission, which should be considered together with any forward-looking statement. No forward-looking statement is a guarantee of future results or events, and one should avoid placing undue reliance on such statements. Anavex Life Sciences Corp. undertakes no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise. Anavex Life Sciences Corp. cannot be sure when or if it will be permitted by regulatory agencies to undertake clinical trials or to commence any particular phase of any clinical trials. Because of this, statements regarding the expected timing of clinical trials cannot be regarded as actual predictions of when Anavex Life Sciences Corp. will obtain regulatory approval for any “phase” of clinical trials. We also cannot be sure of the clinical outcome for efficacy or safety of our compounds. Potential investors should refer to the risk factors in our reports filed on Edgar.

ANAVEX Platform for Neurological Diseases

Neurological chronic conditions:
Impaired restoration function and impaired homeostasis

SIGMAR1 activation as compensatory mechanism to chronic CNS diseases[1]

[1] *Brimson JM, Brimson S, Chomchoei C, et al. Using Sigma-ligands as part of a multi-receptor approach to target diseases of the brain. Expert opinion on therapeutic targets. 2020*

Large Markets by Applying Precision Medicine Platform

Today

- SIGMAR1 activation established as a New Platform Class

- ANAVEX®2-73 (*blarcamesine*) Clinical study results in broad CNS indications confirm SIGMAR1 technology

Tomorrow

- SIGMAR1 technology to Succeed Traditional Modalities

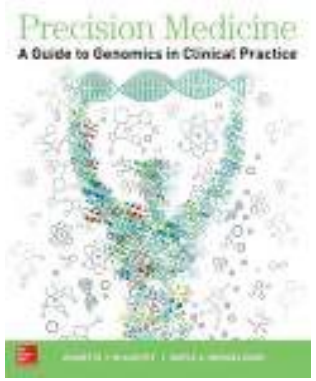
  - Alzheimer's disease
  - Parkinson's disease
  - Rett syndrome
  - Fragile X syndrome
  - Other rare diseases

The Future

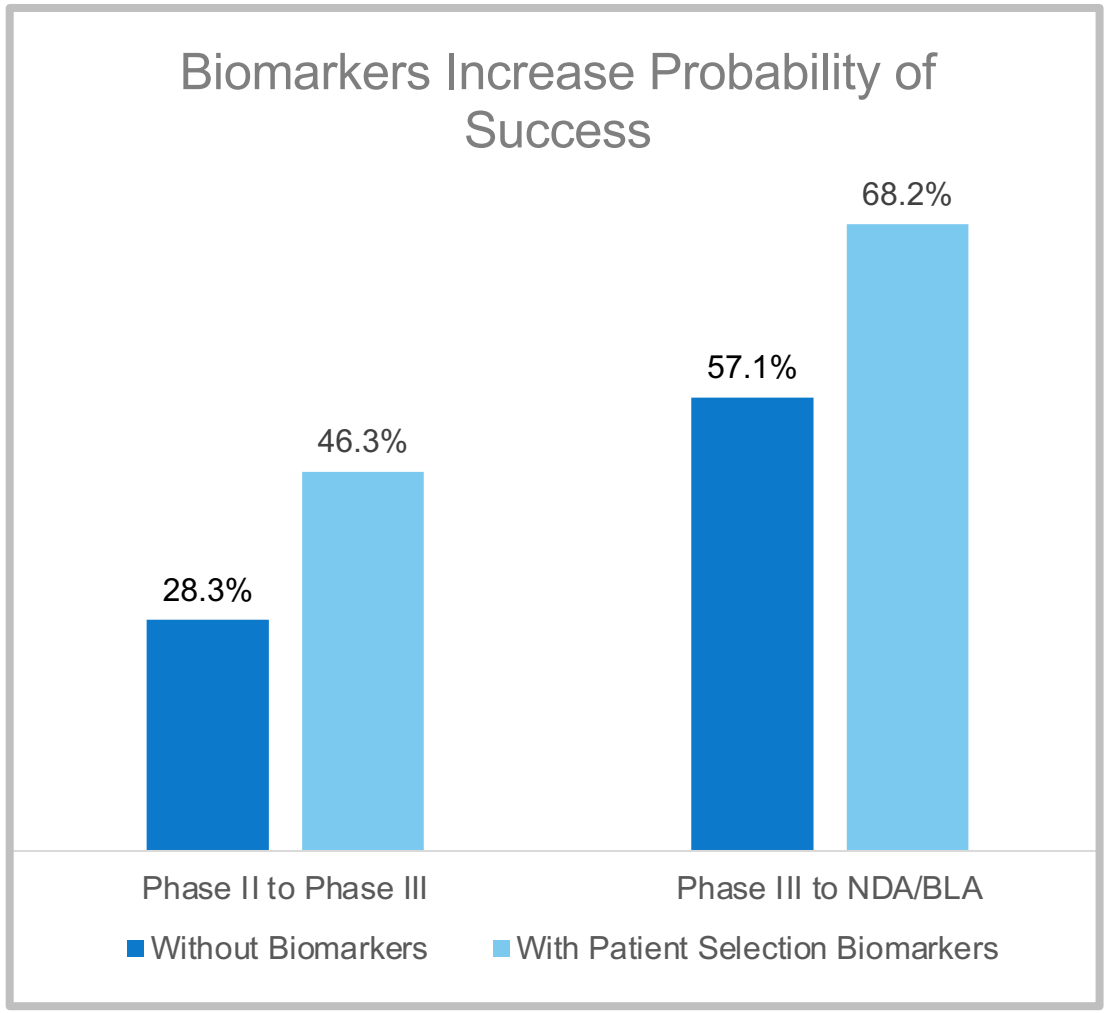
- SIGMAR1 to open up new opportunities Beyond the Horizon

  - Expanded CNS indications
  - Regenerative medicine[1]
  - Disease prevention[2]

[1] K. Ruscher, T. Wieloch, The involvement of the sigma-1 receptor in neurodegeneration and neurorestoration, Journal of Pharmacological Sciences, Volume 127, Issue 1, 2015, Pages 30-35, ISSN 1347-8613, https://doi.org/10.1016/j.jphs.2014.11.011. [2] L. Nguyen et al., Role of sigma-1 receptors in neurodegenerative diseases, Journal of Pharmacological Sciences, Volume 127, Issue 1, 2015, Pages 17-29, ISSN 1347-8613, https://doi.org/10.1016/j.jphs.2014.12.005.



Precision Medicine

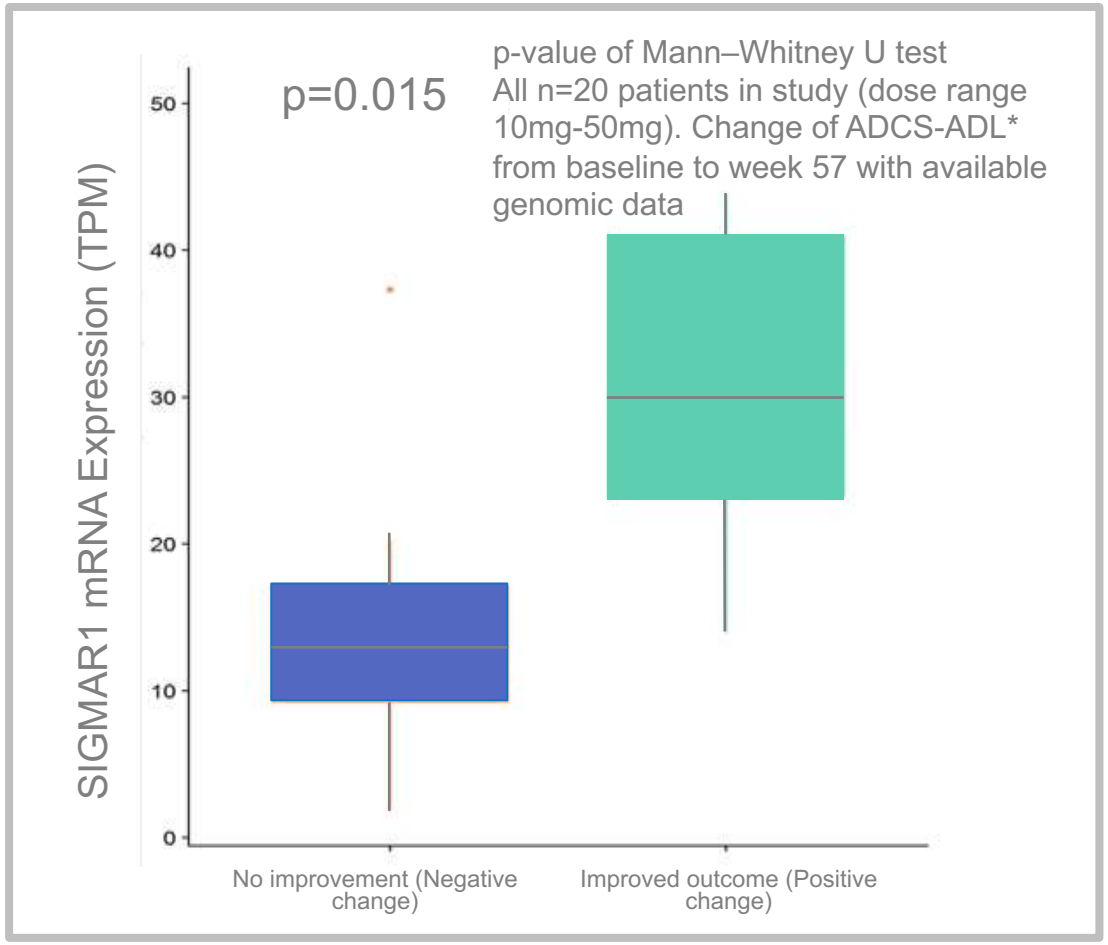


- Patient selection biomarkers
- Higher therapeutic response
- Lower variability in the target population

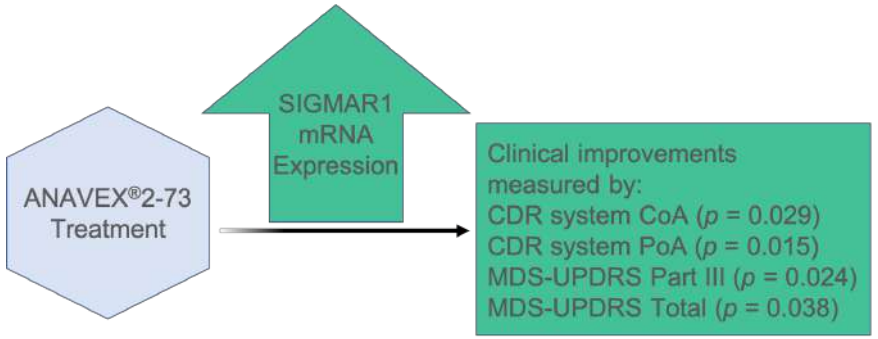
Thomas DW et al. Clinical Development Success Rates 2011-2020. BIO | QLS Advisors | Informa UK Ltd 2021

ANAVEX®2-73 Establishes SIGMAR1 mRNA Predictive Biomarker of Efficacy in Alzheimer's, Parkinson's and Rett Syndrome

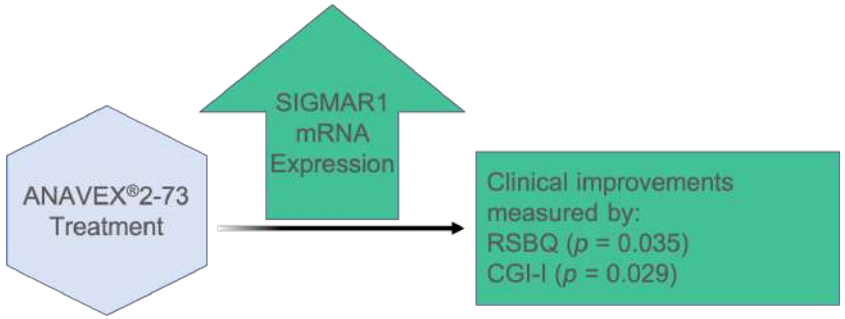
ANAVEX®2-73 improves functional (ADCS-ADL*) outcome in Alzheimer's disease patients correlating with SIGMAR1 mRNA levels



ANAVEX®2-73 positive response in functional outcome in patients with Parkinson's disease correlate with SIGMAR1 mRNA levels



ANAVEX®2-73 positive response in functional outcome in patients with Rett syndrome correlate with SIGMAR1 mRNA levels

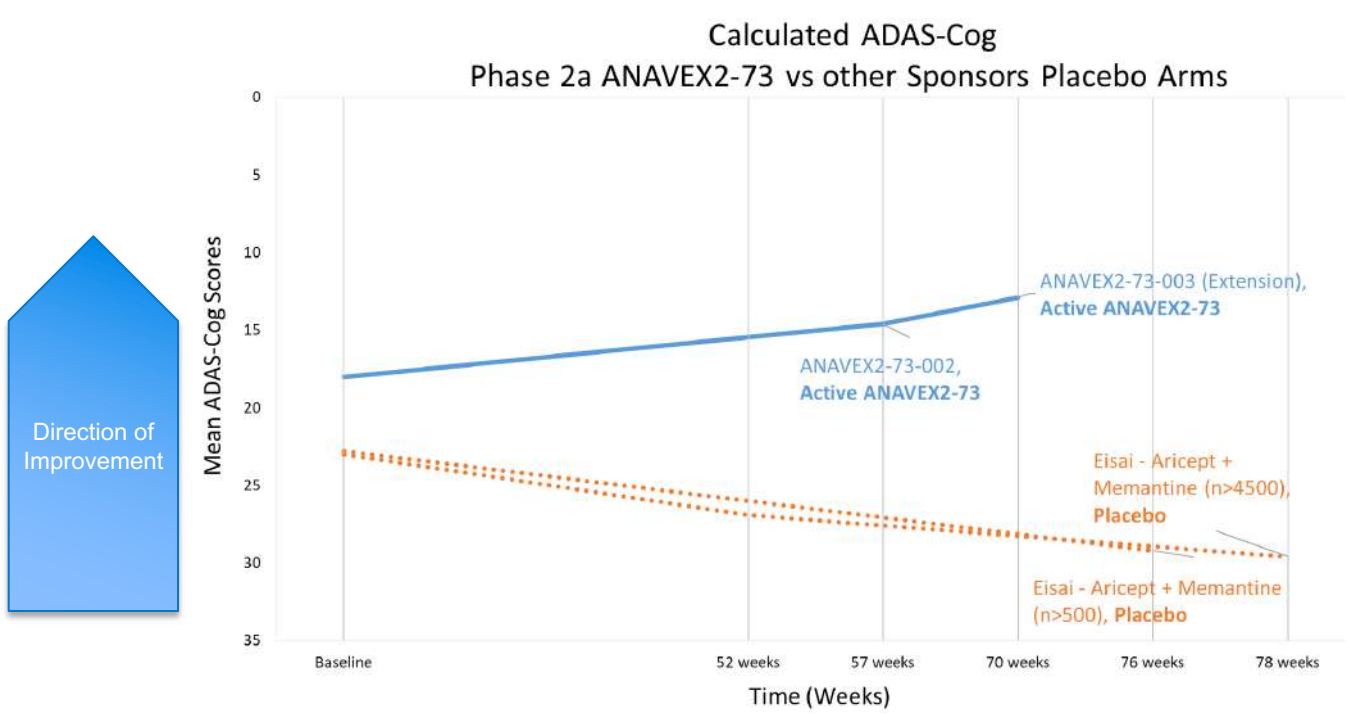


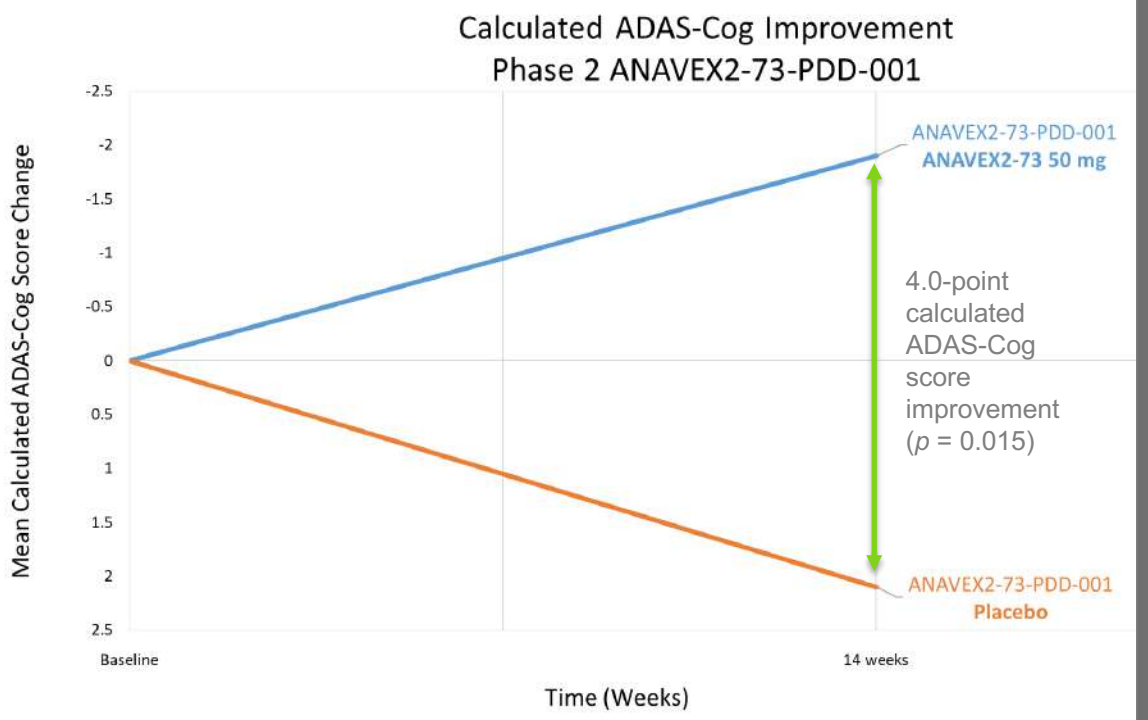
*Source: Hampel H et al. Alzheimer's Dement. 2020;00:1–14; *Alzheimer's Disease Cooperative Study Activities of Daily Living 23-item scale (ADCS-ADL)*

Aiming to Change the Course of Dementia …

… Dementia is progressive and over time a patient's cognition will worsen

▸ Trajectory changed with ANAVEX®2-73



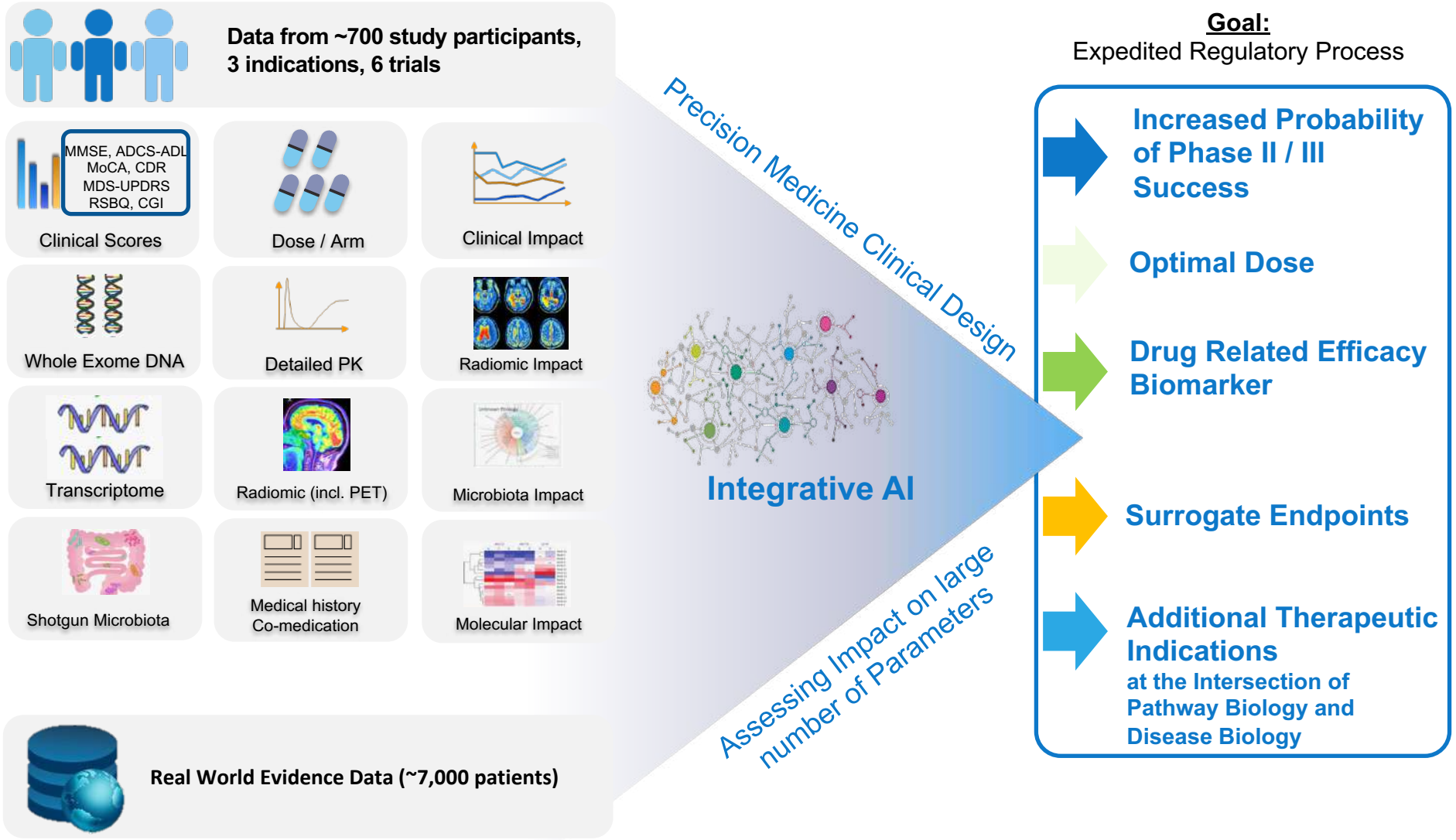


Visualize the improvement in calculated ADAS-Cog scores in Alzheimer's patients treated with ANAVEX®2-73, relative to the placebo arms of other sponsors' trials

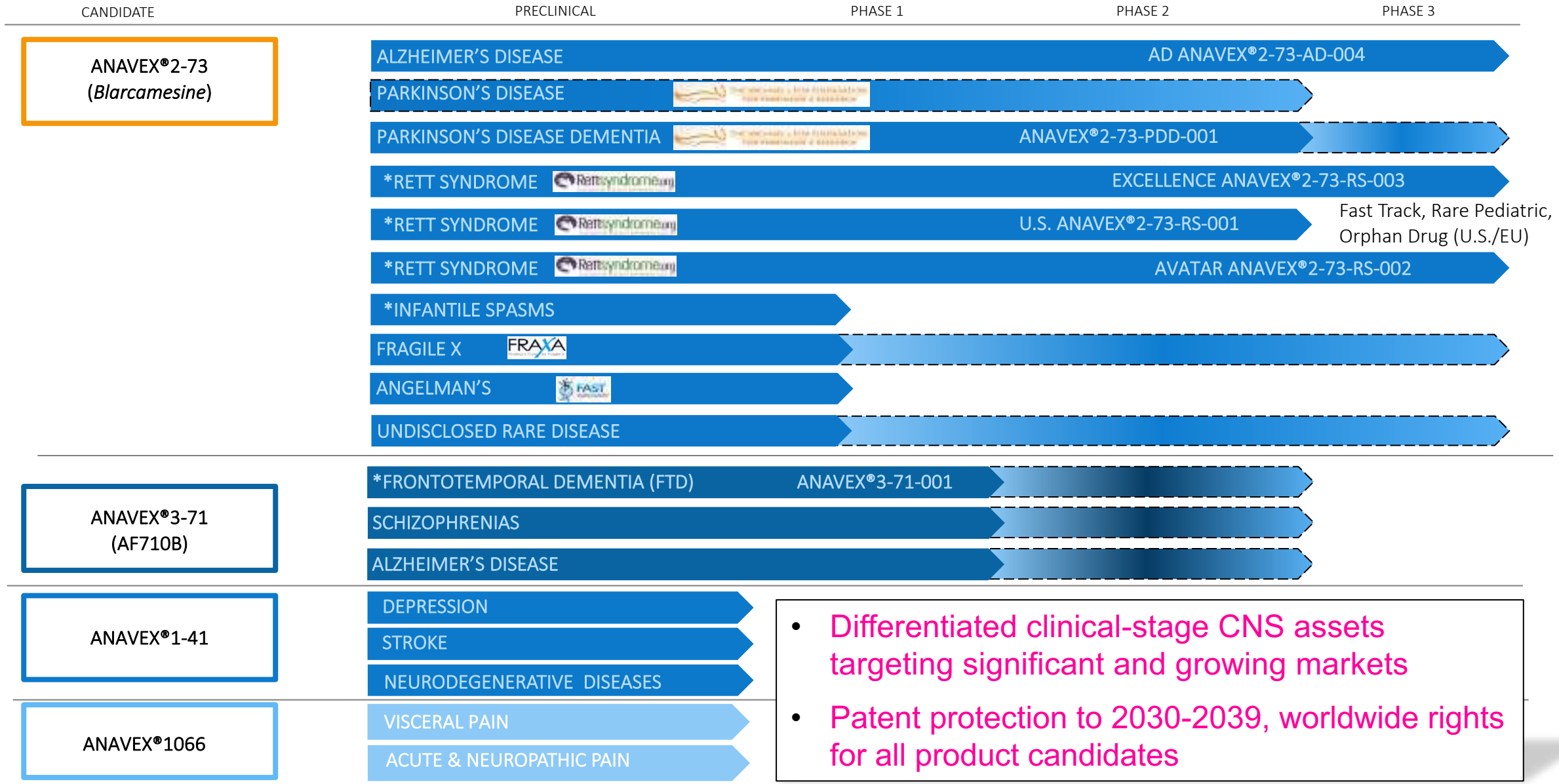
Parkinson's disease dementia (PDD) patients improved with ANAVEX®2-73 in calculated corresponding ADAS-Cog scores from baseline to 14 weeks

Source: https://www.anavex.com/anavex-life-sciences-reports-anavex2-73-blarcamesine-featured-as-a-disease-modifying-small-molecule-in-phase-3-clinical-trials-in-a-new-publication-in-medical-journal-titled-future-av/

AI Powered, Biomarker Driven, Accelerated Development Built on in-depth Molecular Understanding of SIGMAR1 Pathway



Broad SIGMAR1 Platform Targeting Significant Unmet Medical Need

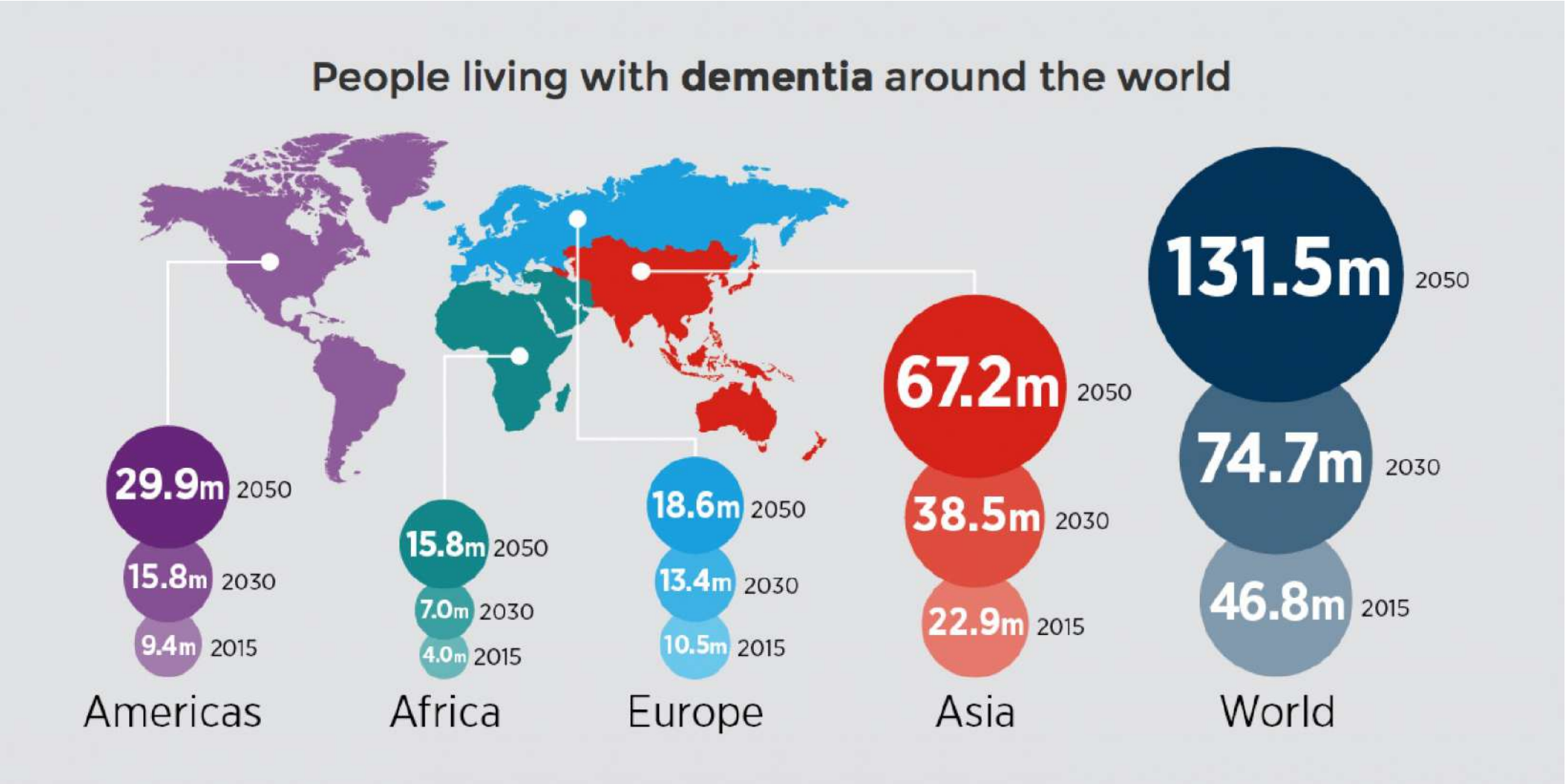


- Differentiated clinical-stage CNS assets targeting significant and growing markets
- Patent protection to 2030-2039, worldwide rights for all product candidates

** = Orphan Drug Designation by FDA; Dashed lines indicate planned clinical studies*

Worldwide Dementia Cases Projected to Grow to Over 130M by 2050

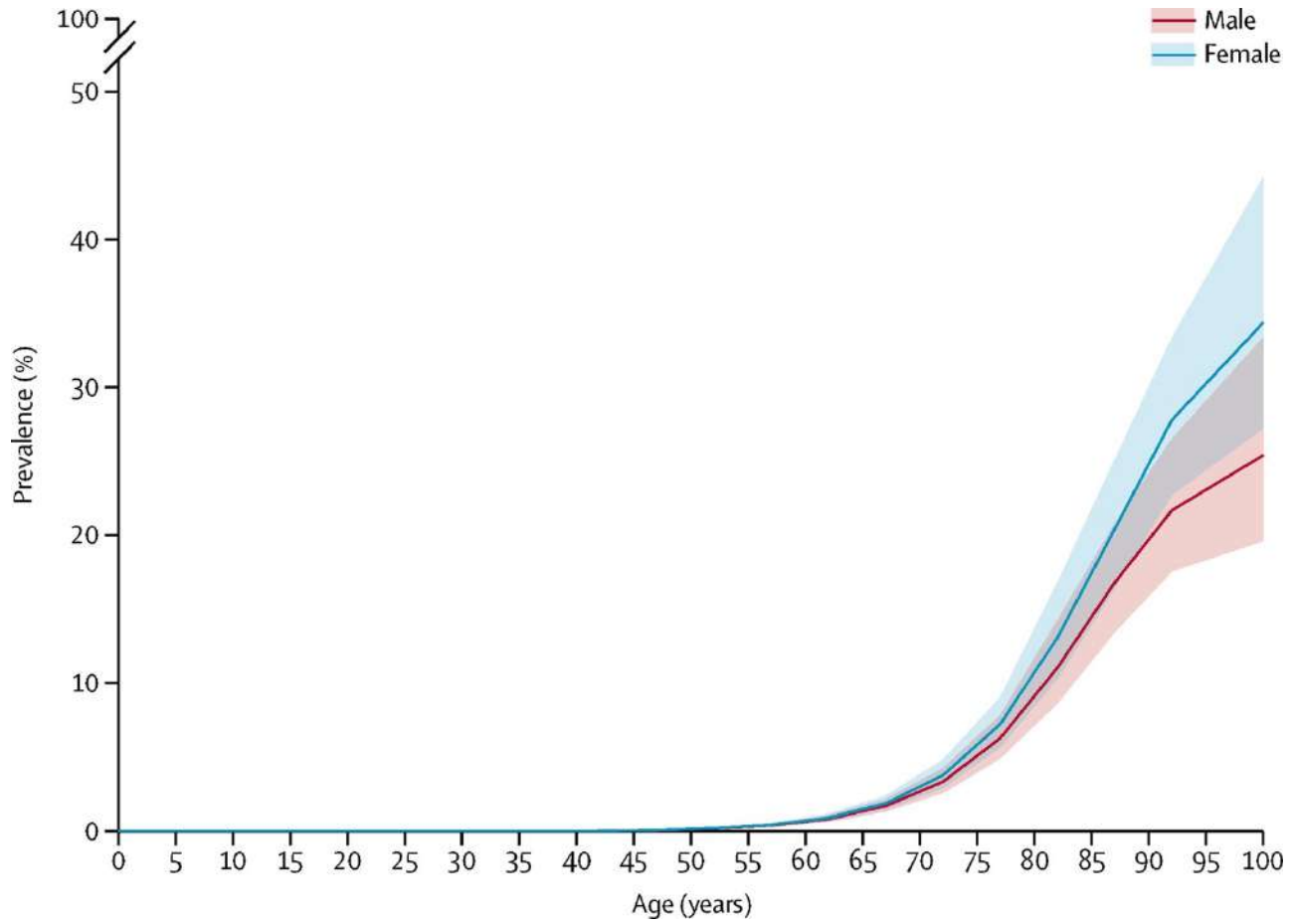
Targeting Large Market: Global Dementia



Source: World Alzheimer's Report

Costs Associated with Alzheimer's Treatment and Care in the U.S. are Unsustainable

Age Prevalence of Global Alzheimer's Disease and Dementias



>$20 trillion

Cumulative costs of Alzheimer's and dementia care from 2015 to 2050

1 in 3

Medicare dollars will be spent on people living with Alzheimer's and other dementias in 2050

>11 million

The number of Americans providing unpaid care for people with Alzheimer's or other dementias

Source: GBD 2016 Dementia Collaborators. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan;18(1):88-106; www.alz.org

Targeting Large Market Opportunities with Significant Unmet Medical Need

U.S. and Global Patient Numbers

Indication	USA	Europe	Asia	Global
Alzheimer's Disease (AD)[1,2]	~5,700,000	~7,800,000	~23,000,000	~35,000,000
Parkinson's Disease (PD)[3,4]	~1,000,000	~1,400,000	~3,000,000	~10,000,000
Frontotemporal Dementia (FTD)[5]	~60,000	~65,000	~500,000	~800,000
Schizophrenias[6,7*]	~1,500,000	~3,000,000	~6,000,000	~20,000,000
Rett Syndrome (RTT)[8*]	~11,000	~13,000	~37,000	~350,000
Fragile X Syndrome (FXS)[9,10*]	~62,500	~150,000	~900,000	~1,400,000

1) *Alzheimer's Disease Facts and Figures. Alzheimers Dement 2018;14(3):367-429*
2) *Dementia in the Asia Pacific Region. Alzheimer's Disease International 2014; 10*
3) *Marras C et al 2018. npj Parkinson's Disease volume 4, Article number: 21*
4) *GBD 2016 Parkinson's Disease Collaborators. The Lancet 2018 Volume 17, Issue 11, P3939-953*
5) *Knopman & Roberts 2011. J Mol Neurosci 2011;45(3):330-335*
6) *National Alliance on Mental Illness, 2019*
7) *Fasseh et al., 2018. Eur J Public Health. 2018 Dec 1;28(6):1043-1049*
8) *Rettsyndrome.org, 2016*
9) *National Fragile X Foundation, 2022*
10) *Hunter et al., 2014. Am J Med Genet A. 2014 Jul;164A(7):1648-5*

** Patient estimates derived from the published prevalence estimate range for the regional population*

Anavex's Transformative Precision Medicine Platform

- ANAVEX®2-73 (*Blarcamesine*) Rett Syndrome Program Received Fast Track Designation and is Eligible for Pediatric Priority Review Voucher
- Pursuing Large Markets with High Unmet Need by Applying Genetic Precision Medicine
- Novel Upstream CNS Mechanism of Action for both Neurodevelopment and Neurodegeneration
- Compelling Human Patient Data in Rett Syndrome (RTT), Parkinson's Disease Dementia (PDD) and Alzheimer's Disease (AD)
- Sufficient Cash for >5 Years To Achieve Key Milestones – Including non-dilutive Cash from Michael J Fox Foundation, International Rett Syndrome Foundation and Australian Government

Continued Significant Value-creating Pipeline Expansion Opportunities for ANAVEX®2-73:

- Novel approach of targeting SIGMAR1 using precision medicine with potential for biomarker-focused pivotal Fragile X and Parkinson's disease dementia clinical trials

Catalysts to Drive Value

The company has multiple clinical milestones

- ✅ Complete data ANAVEX®2-73 U.S. adult Rett syndrome (RTT) Phase 2 study
- ✅ Complete data ANAVEX®2-73 Parkinson's disease dementia (PDD) Phase 2 study
- ✅ Top-line data Phase 1 ANAVEX®3-71 clinical trial
- ✅ Top-line data AVATAR: Potentially pivotal Phase 3 adult RTT ANAVEX®2-73 clinical trial
- 〉 Top-line data ANAVEX®2-73-AD-004: Potentially pivotal Phase 2b/3 AD clinical trial – expected 2H 2022
- 〉 Top-line data EXCELLENCE: Potentially pivotal Phase 2/3 pediatric RTT clinical trial – expected 2H 2022
- 〉 Initiation of ANAVEX®2-73 imaging-focused Parkinson's disease clinical trial – expected 2022
- 〉 Initiation of potentially pivotal ANAVEX®2-73 Phase 2/3 Fragile X clinical trial – expected 2022
- 〉 Initiation of potentially pivotal ANAVEX®2-73 Phase 2/3 clinical trial for the treatment of a new, rare disease indication – expected 2022
- 〉 Initiation of ANAVEX®3-71 Phase 2 clinical trial for FTD, schizophrenias and Alzheimer's disease – expected 2022

ANAVEX®2-73 Clinical Trials
Mechanism of Action (MoA) and Clinical Data:

- Rett Syndrome (RTT)
- Parkinson’s Disease Dementia (PDD)
- Alzheimer’s Disease (AD)

SIGMAR1 Activation has been Shown to Modulate Multiple Aspects of Neurodegenerative Processes

Sigma-1 receptor agonists have been shown to restore neuronal functions in neurodegenerative processes

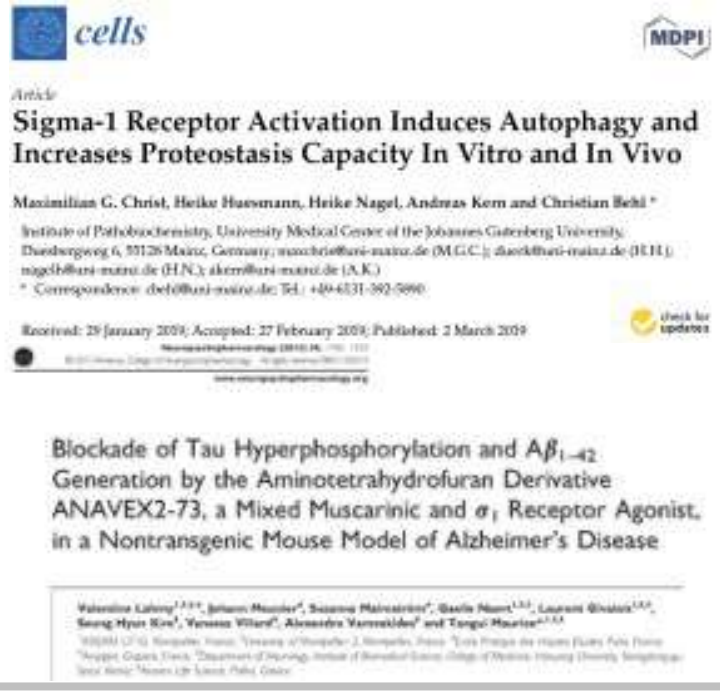

Journal of Pharmacological Sciences

Critical review

Role of sigma-1 receptors in neurodegenerative diseases

Linda Nguyen, Brandon P. Lucke-Wold, Shona A. Mookerjee, John Z. Cavendish, Matthew J. Robson, Anna L. Scandinaro, Rae R. Matsumoto

ANAVEX®2-73 enhances autophagy and alleviates Tau pathology in neurodegenerative disease models


cells

MDPI

Article

Sigma-1 Receptor Activation Induces Autophagy and Increases Proteostasis Capacity In Vitro and In Vivo

Maximilian G. Christ, Heike Huesmann, Heike Nagel, Andreas Kern and Christian Behl

Blockade of Tau Hyperphosphorylation and $A\beta_{1-42}$ Generation by the Aminotetrahydrofuran Derivative ANAVEX2-73, a Mixed Muscarinic and σ_1 Receptor Agonist, in a Nontransgenic Mouse Model of Alzheimer's Disease

Sigma-1 receptor agonists have a neuroprotective effect in neurodegenerative disease models


REVIEW ARTICLE

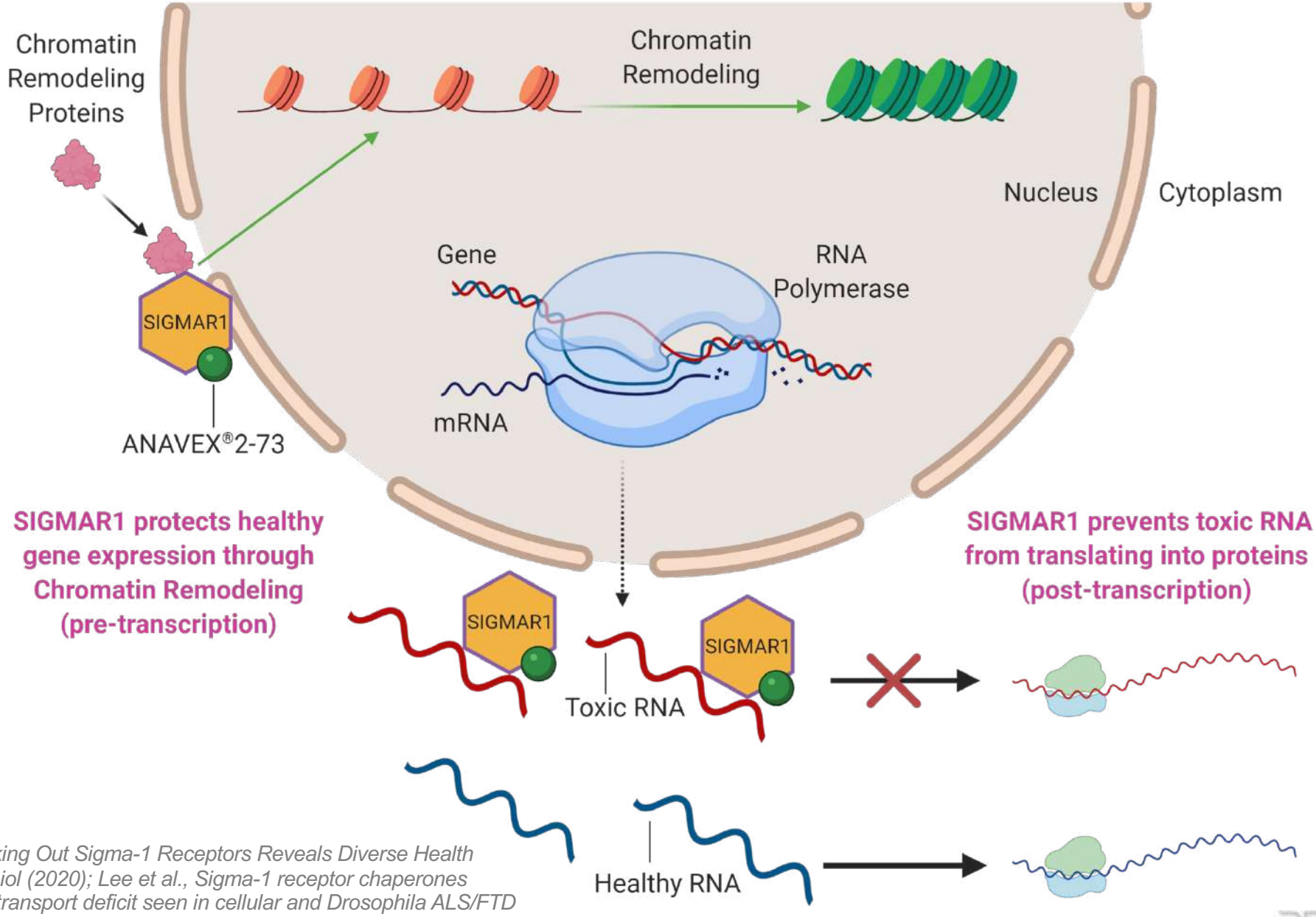
Neuronal Sigma-1 receptors: signaling functions and protective roles in neurodegenerative diseases

Daniel A. Ryskamp, Svetlana Korban, Vladimir Zhemkov, Nina Kraskovskaya and Ilya Bezprozvanny

Neuroprotective effects of sigma-1 receptor agonists against beta-amyloid-induced toxicity

Agostino Marrazzo, Filippo Caraci, Elisa Trovato Salinaro, Teung-Ping Su, Agata Copani and Giuseppe Ronsisvalle

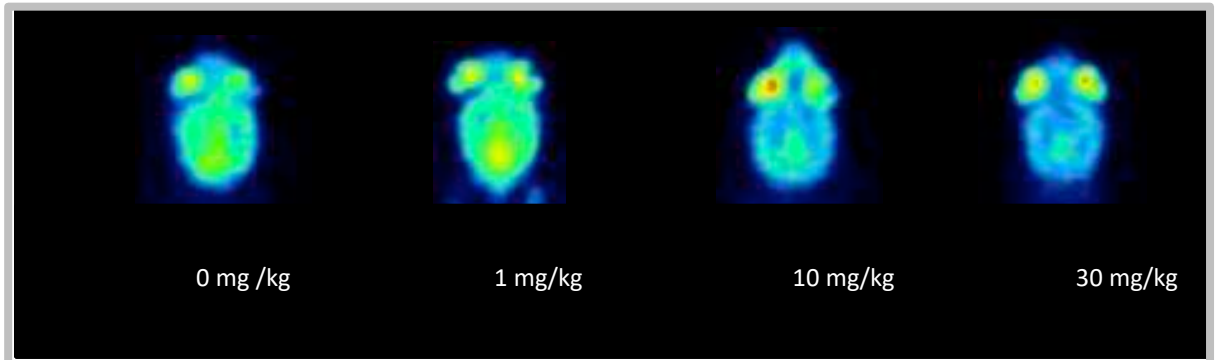
ANAVEX®2-73 MoA: SIGMAR1 Activation Prevents Cellular Stress Before *and* After RNA Gene Transcription

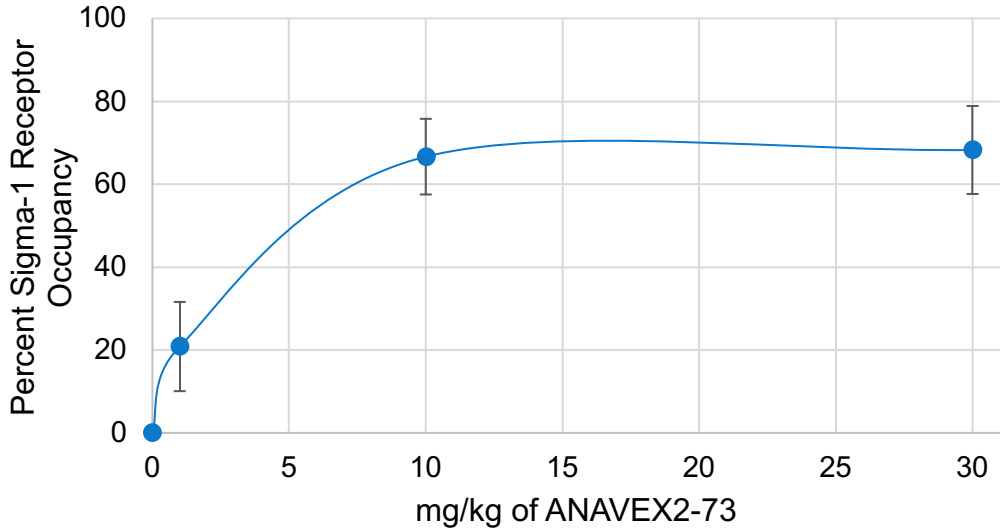


Source: Couly et al., Knocking Out Sigma-1 Receptors Reveals Diverse Health Problems. Cell Mol Neurobiol (2020); Lee et al., Sigma-1 receptor chaperones rescue nucleocytoplasmic transport deficit seen in cellular and Drosophila ALS/FTD models. Nat Commun. 2020 Nov 4;11(1):5580

ANAVEX®2-73 Establishes Proof-of-Concept and SIGMAR1 Target Occupancy

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





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

What is Rett Syndrome?

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

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
  - The population of patients with Rett syndrome is estimated to be ~11,000 patients in the U.S.
  - There is currently no cure for Rett syndrome

Source: https://www.rettsyndrome.org/about-rett-syndrome

ANAVEX® Rett Syndrome Program

Completed and ongoing late-stage clinical studies for Rett Syndrome in 2022:

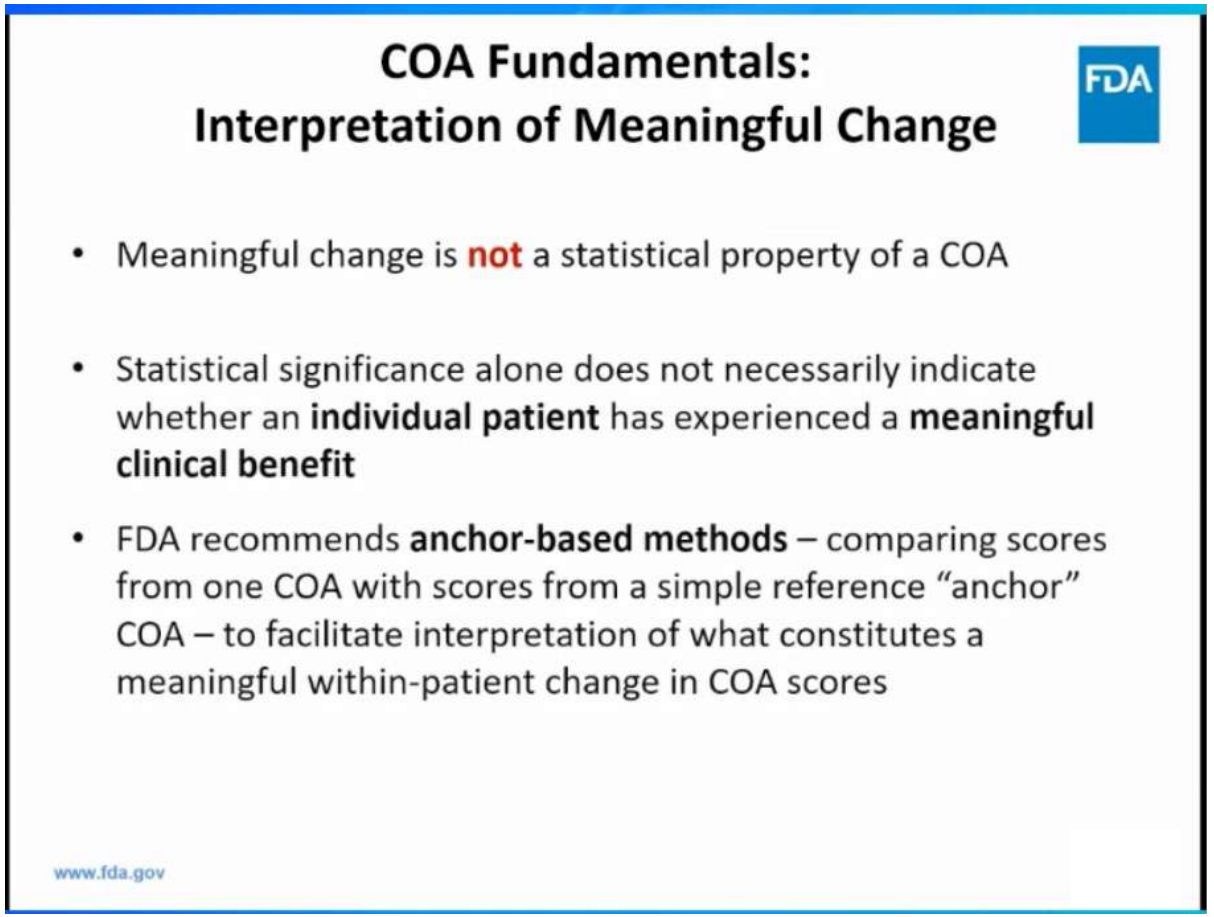
- U.S. Phase 2 Adult Rett Syndrome Trial (ClinicalTrials.gov Identifier: NCT03758924) - *completed*
- AVATAR Phase 3 Adult Rett Syndrome Trial (ClinicalTrials.gov Identifier: NCT03941444) - *completed*
- EXCELLENCE Phase 2/3 Pediatric Rett Syndrome Trial (ClinicalTrials.gov Identifier: NCT04304482) - *ongoing*
- ANAVEX®2-73 Rett Syndrome Program Received Fast Track Designation, Orphan Drug Designation and Rare Pediatric Disease Designation

Pivotal Efficacy	Supportive Efficacy	Safety Database
• Positive Phase 3 AVATAR Study	• Positive Phase 2 U.S. Rett Syndrome Study	• Safety and Tolerability Data from Completed & Ongoing Studies

Appropriate Primary Endpoint for Rett Syndrome

Background for Meaningful Trial Endpoint (COA)[1]

- Statistical significance alone not sufficient for determining whether an individual patient has experienced a *meaningful* clinical benefit
- FDA recommends:
  - **Anchor-based responder method**[2] – linking of scores from one clinical outcome assessment (e.g., RSBQ)[3] with scores from a simple reference "anchor" clinical outcome assessment with a **clinically meaningful threshold** (e.g., CGI-I)[4] to facilitate interpretation of what constitutes a meaningful within and between patient change in clinical outcome assessment scores (e.g., RSBQ AUC)[5]



1) *COA = Clinical Outcome Assessment*
2) *Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims*
3) *RSBQ = Rett Syndrome Behavioural Questionnaire*
4) *CGI-I = Clinical Global Impression of Improvement*
5) *AUC = Area Under the Effective Curve is a composite measure of treatment effect disease progression and symptoms*

ADAMS Scale and CGI-I Scale

Anxiety, Depression, and Mood Scale (ADAMS) and Clinical Global Impression of Improvement (CGI-I)

- The Anxiety, Depression, and Mood Scale (ADAMS) is a measure of anxiety and mood symptoms in individuals with intellectual disability.[1] It has been clinically validated for use in Rett syndrome[2] and in Fragile X syndrome[3]
- The ADAMS generates a total score and 5 subscale scores:
  - Manic/hyperactive behavior
  - Depressed mood
  - Social avoidance
  - General anxiety
  - Obsessive compulsive behavior

- The Clinical Global Impression of Improvement Scale (CGI-I) is a measure developed for use in clinical trials to provide a brief, stand-alone assessment of the clinician's view of the patient's global functioning prior to and after initiating a study medication. Each time the patient is seen after medication has been initiated, the clinician compares the patient's overall clinical condition to the period just prior to the initiation of medication use (the so-called baseline visit).[4]

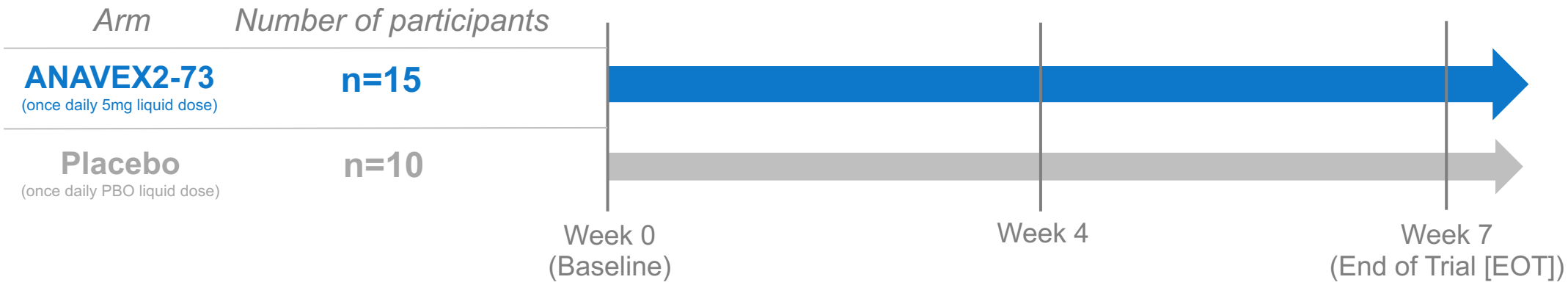
Clinically Meaningful

❌	❌	❌	❌	✅	✅	✅
7	6	5	4	3	2	1
Very Much Worse	Much Worse	Minimally Worse	No Change	Minimally Improved	Much Improved	Very Much Improved

1) Esbensen AJ, Rojahn J, Aman MG, Ruedrich S. Reliability and validity of an assessment instrument for anxiety, depression, and mood among individuals with mental retardation. J Autism Dev Disord. 2003;33:617–29 Kluwer Academic Publishers-Plenum Publishers; 2) Barnes KV, Coughlin FR, O'Leary HM, Bruck N, Bazin GA, Beinecke EB, Walco AC, Cantwell NG, Kaufmann WE. Anxiety-like behavior in Rett syndrome: characteristics and assessment by anxiety scales, J Neurodev Disord. 2015;7(1):30. doi: 10.1186/s11689-015-9127-4. Epub 2015 Sep 15; 3) Cordeiro L, Ballinger E, Hagerman R, Hessl D. Clinical assessment of DSM-IV anxiety disorders in fragile X syndrome: prevalence and characterization. J Neurodev Disord. 2011;3:57–67; 4) Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. Psychiatry (Edgmont). 2007;4(7):28-37.

Rett Syndrome U.S. ANAVEX®2-73-RS-001 Phase 2 Trial Design Overview

Randomized, Double-blind, Placebo-controlled Clinical Trial



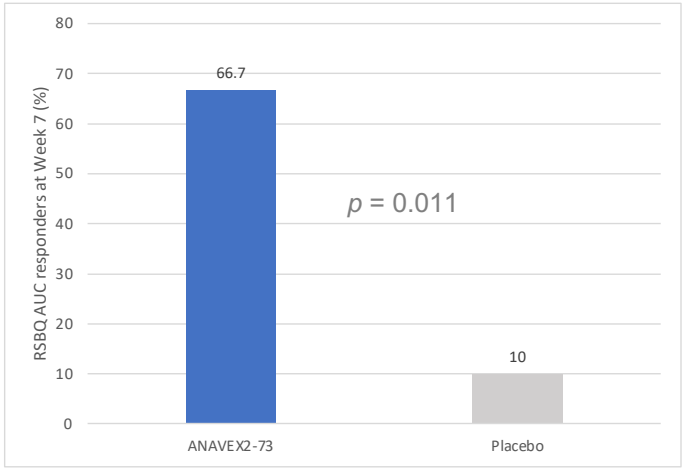
Assessments:

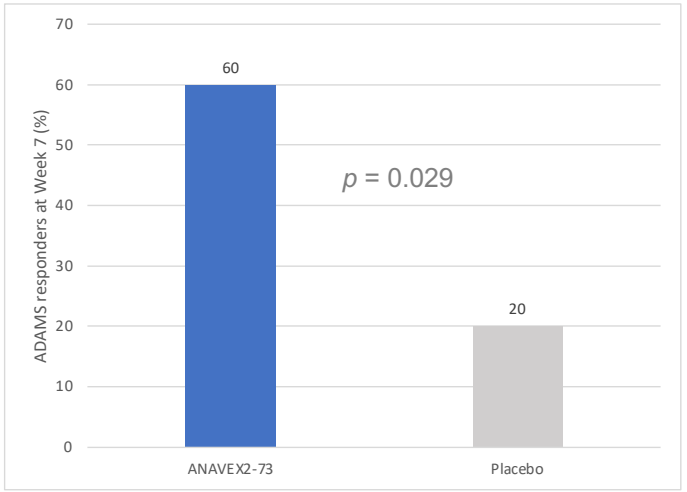
- Primary: Safety
- Secondary: RSBQ (Rett Syndrome Behaviour Questionnaire) AUC response, Behavior ADAMS (Anxiety, Depression, and Mood Scale) response, CGI-I (Clinical Global Impression – Improvement) response, Sleep (CSHQ), VAS (top caregiver concerns), Seizure diary
- Biomarkers of response and/or surrogate endpoints: Genomic biomarker: DNA & mRNA profiles and metabolomics biomarkers
- *SIGMAR1* variants: Prespecified analyses of population with wild type (WT) variant

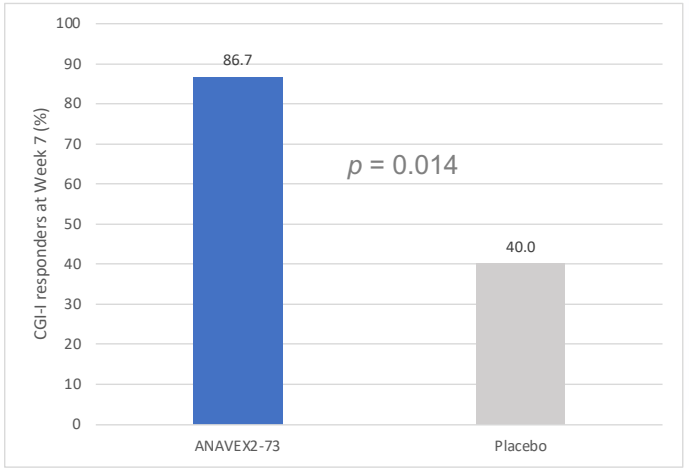
ClinicalTrials.gov: NCT03758924
Separate patient cohort (n=6) underwent a 7-week intensive pharmacokinetic (PK) assessment with safety, tolerability, pharmacokinetic and efficacy evaluation of ANAVEX®2-73
Open-label-extension after End of Trial for at least 36 weeks

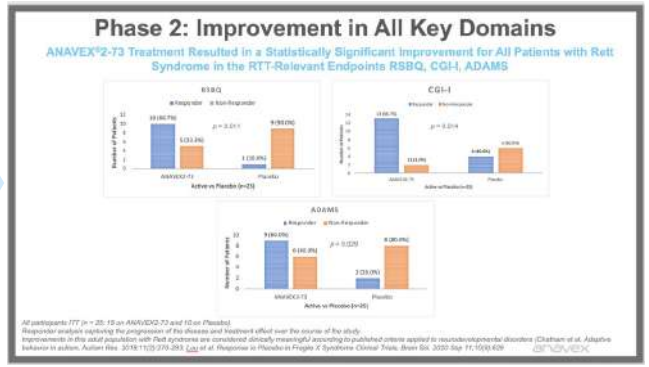
U.S. RTT Phase 2: Improvement in All Key Domains

ANAVEX®2-73 Treatment Resulted in a Statistically Significant Improvement for All Patients with Rett Syndrome in the RTT-Relevant Endpoints of RSBQ AUC[1,2], ADAMS[2], CGI-I[2] responses









RTT efficacy endpoints consistent since December 15, 2020

ITT (n = 25)

[1] CGI-I anchored RSBQ AUC responder analysis capturing the progression of the disease and treatment effect over the course of the study; [2] Improvement threshold of at least 1 full point in the CGI-I scale from 'No Change' (i.e., 4) to at least 'Minimally Improved' (i.e., 3) or 'Much Improved' (i.e., 2) or 'Very Much Improved' (i.e., 1)

Phase 3 AVATAR ANAVEX®2-73-RS-002 Trial in Adult Patients with Rett Syndrome - Design Overview

Randomized, Double-blind, Placebo-controlled Multi-center Clinical Trial

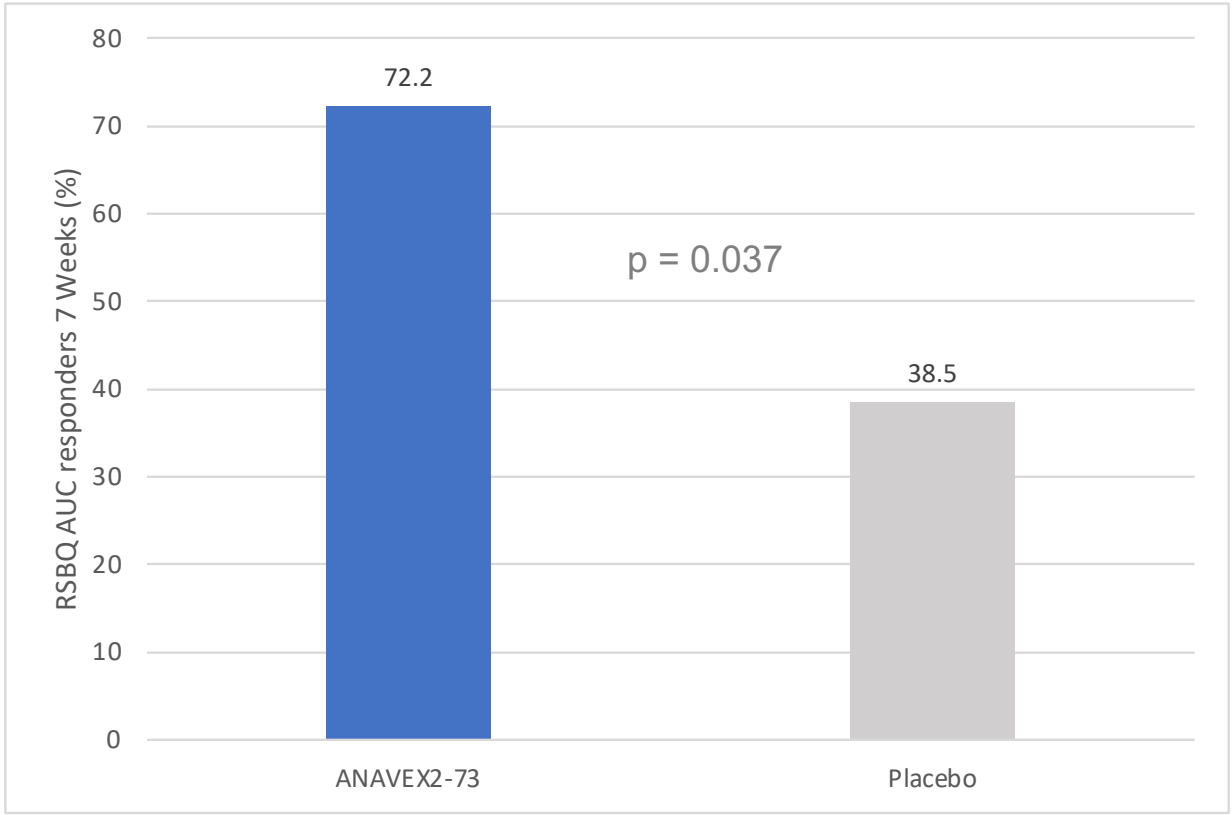
Assessments:

- Primary: RSBQ AUC response and safety
- Secondary: Behavior (ADAMS) response and CGI-I (Clinical Global Impression of Improvement) response
- Exploratory: Sleep (CSHQ), VAS (top caregiver concerns), Child Health Questionnaire PF50 (CHQ-PF50), Rett syndrome Caregiver Inventory Assessment (RTT-CIA), Seizure diary
- Biomarkers of response and/or surrogate endpoints: DNA & mRNA profiles and metabolomics biomarkers
- *SIGMAR1* variants: Prespecified analyses of population with wild type (WT) variant

ClinicalTrials.gov: NCT03941444
Separate patient cohort (n=3) underwent a 3-week intensive pharmacokinetic (PK) assessment with safety, tolerability, pharmacokinetic and efficacy evaluation of ANAVEX®2-73
Open-label-extension (OLE) after End of Trial for at least 48 weeks

Primary Endpoint

Primary Efficacy Endpoint



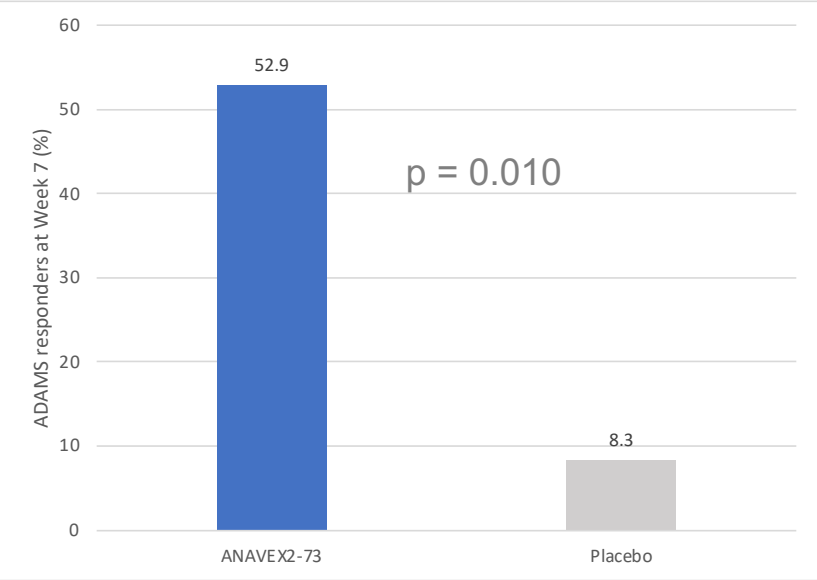
- Oral administration of ANAVEX®2-73 causes a clinical meaningful improvement of RSBQ AUC* in 72.2% of patients as compared to 38.5% on placebo; (p = 0.037)
- Cohen's d effect size 1.91 (very large)

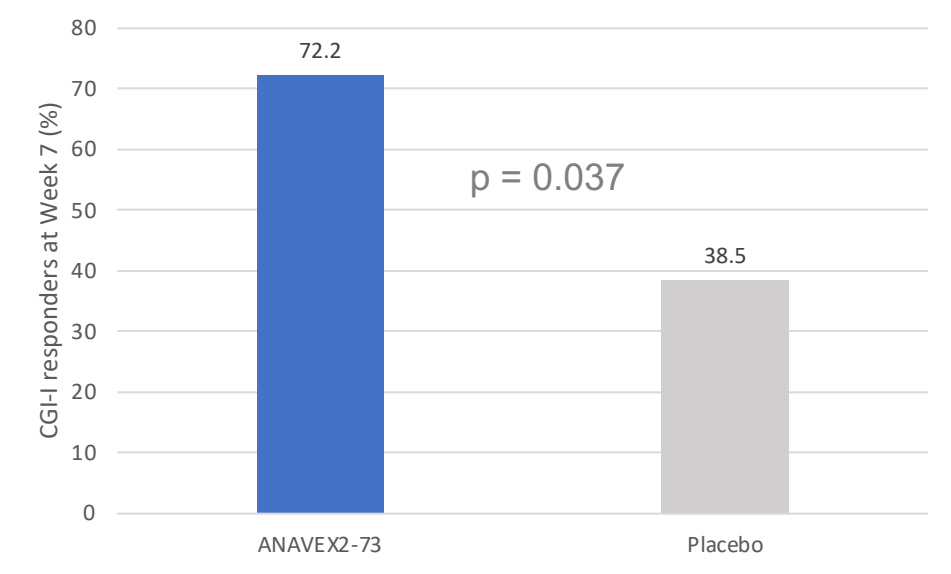
ITT (n = 31)

** Improvement threshold of at least 1 full point in the CGI-I scale from 'No Change' (i.e., 4) to at least 'Minimally Improved' (i.e., 3) or 'Much Improved' (i.e., 2) or 'Very Much Improved' (i.e., 1)*

Secondary Endpoints

Secondary Efficacy Endpoints ADAMS and CGI-I





- Clinically meaningful and statistically significant reduction of emotional behavioral symptoms (ADAMS) response* for ANAVEX®2-73 treated adult patients with Rett syndrome (52.9%) vs placebo (8.3%); (p = 0.010)
- Cohen's d effect size 0.609 (large)

** Improvement threshold of at least -20% change (improvement) of ADAMS total score from baseline*

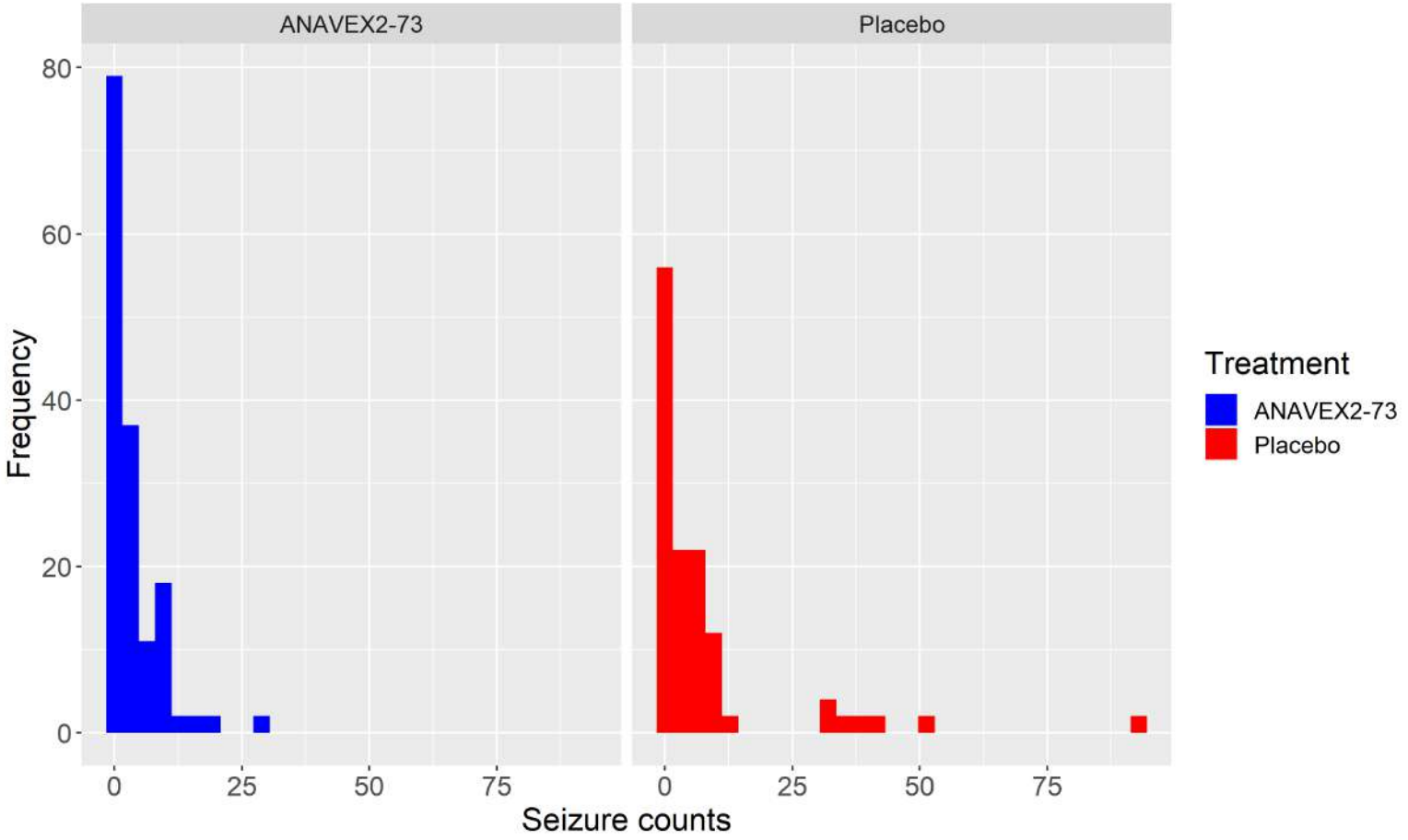
- Significantly more patients achieve clinically meaningful CGI-I response** over the treatment duration in ANAVEX®2-73-treated group (72.2%) as compared with placebo (38.5%); (p = 0.037)
- Cohen's d effect size 1.91 (very large)

*** Improvement threshold of at least 1 full point in the CGI-I scale from 'No Change' (i.e., 4) to at least 'Minimally Improved' (i.e., 3) or 'Much Improved' (i.e., 2) or 'Very Much Improved' (i.e., 1)*

Other Endpoints

Quality of Life (QoL) Assessment and Distribution of Seizure Count by Treatment Arm

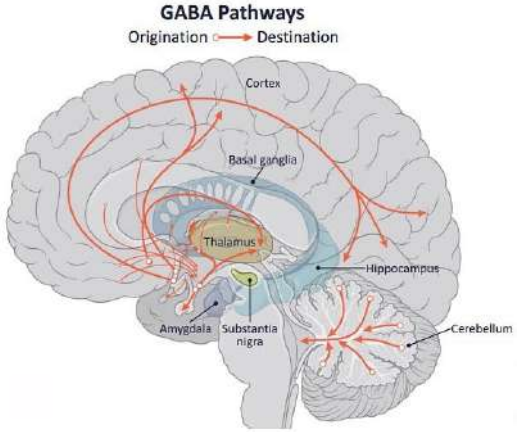
- Child Health Questionnaire-Parent Form 50 (CHQ-PF50)
- The CHQ-PF50 is an internationally recognized general health-related global measure of Quality of Life (QoL) encompassing physical and psychosocial concepts (physical function, psychosocial, behavior, bodily pain, emotional impact, family activities, family cohesion, and general health perception)
- ANAVEX®2-73 demonstrated dose-related significant improvement in overall Quality of Life (QoL) measured with CHQ-PF50 Total Score (p = 0.030)

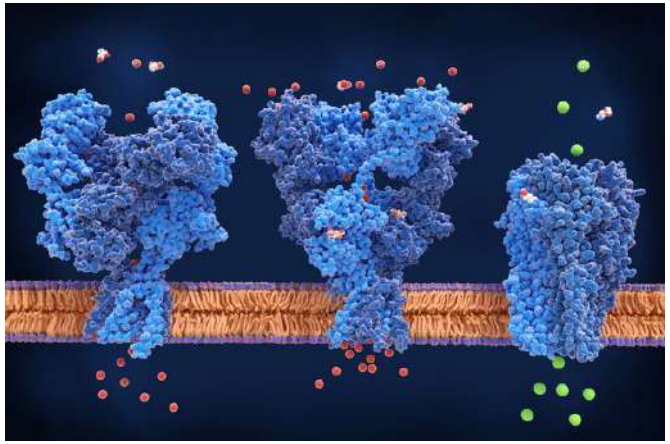


- ANAVEX®2-73 is associated with a 50.7% reduction in weekly seizure risk

GABA a Potential Biomarker, Predicting Clinical Outcome in ANAVEX®2-73 Rett Syndrome Study

- In patients with RTT, *MECP2* deficiency disrupts the GABAergic cycle[1], resulting in *decreased* GABA, and impaired synaptic and mitochondrial function[1,2,3,4,5,6]





- AVATAR efficacy endpoints demonstrated statistically significant and clinically meaningful reductions in Rett syndrome symptoms with related changes in potential biomarkers of disease pathology:
- GABA[7] was significantly *increased* ($p = 0.0205$)
- Gliotoxin L-Alpha-aminoadipic acid (L-AAA)[8] was significantly *decreased* ($p = 0.0392$)

1) Jin et al., 2015; 2) Chao et al., 2020; 3) Hamberger et al., 1992; 4) Lappalainen et al., 1996; 5) Neul et al., 2020 6) Kaufmann et al., 2005
7) Ure K, Lu H, Wang W, et al. Restoration of Mecp2 expression in GABAergic neurons is sufficient to rescue multiple disease features in a mouse model of Rett syndrome. Elife. 2016 Jun 21;5:e14198; 8) Wu HQ, Ungerstedt U, Schwarcz R. L-alpha-aminoadipic acid as a regulator of kynurenic acid production in the hippocampus: a microdialysis study in freely moving rats. Eur J Pharmacol. 1995 Jul 25;281(1):55-61

Safety and Adverse Events During Treatment Period

- ANAVEX®2-73 was well tolerated with very good medication compliance of 95%
- Similar TEAE rates observed in ANAVEX®2-73 and placebo arms
- AEs ≥10% were predominantly mild or moderate
- No clinically significant changes in vital signs, lab values and ECG parameters in ANAVEX®2-73 and placebo groups
- No incidence of diarrhea or vomiting
- Safety findings are consistent with the known safety profile of ANAVEX®2-73

Adverse Events During the Treatment Period		
	ANAVEX®2-73 (n=20)	**Placebo (n=13)**
	number (%)	number (%)
Patients with any TEAE	15 (75.0%)	8 (61.5%)
Patients with a serious TEAE	3 (15.0%)	2 (15.4%)
Patients with a TEAE leading to Study Discontinuation	2 (10.0%)	1 (7.7%)
AEs ≥10%		
Somnolence[1]	4 (20.0%)	2 (15.4%)
Lethargy[2]	4 (20.0%)	0 (0.0%)
Sedation	2 (10.0%)	0 (0.0%)
Constipation	2 (10.0%)	1 (7.7%)
Urinary tract infection	2 (10.0%)	1 (7.7%)
Hypophagia	2 (10.0%)	0 (0.0%)
Skin rash	2 (10.0%)	1 (7.7%)

[1] Medical history of Somnolence in 3 patients; 1 severe, all others mild
[2] All mild

Favorable Adverse Event Profile of ANAVEX®2-73

	Adverse Events (>10%)		
	Diarrhea	Vomiting	Fever (Pyrexia)
ANAVEX2-73 (30 mg)*	0%	0%	0%
trofinetide (400 mg/kg)**	80.7%	27.0%	8.6%

ANAVEX®2-73 AVATAR Phase 3 Adverse Event profile compares favorably with other presented trial

** All participants ITT*

*** Source: www.acadia-pharm.com Lavender™ Study Presentation December 6th 2021, page 28*

ANAVEX®2-73-RS-003 Phase 2/3 Rett Syndrome EXCELLENCE Study

N=84

12 WEEK STUDY

… and Open Label Extension (OLE) **48 weeks**

RTT patient population

- Diagnosis of confirmed RTT
- Patients age 5-17
- DNA and RNA sequencing

Randomization 2:1

- ANAVEX®2-73 **Active dose#**
- Placebo

ClinicalTrials.gov: NCT04304482

Primary and Secondary Endpoints

- RSBQ AUC, CGI-I
- ADAMS, Sleep function
- Seizure activity
- Safety and tolerability of ANAVEX®2-73
- Glutamate biomarker

Pre-specified Analysis

- Excluding genetic variants SIGMAR1 (rs1800866), COMT (rs113895332/rs61143203) with influence on treatment effect

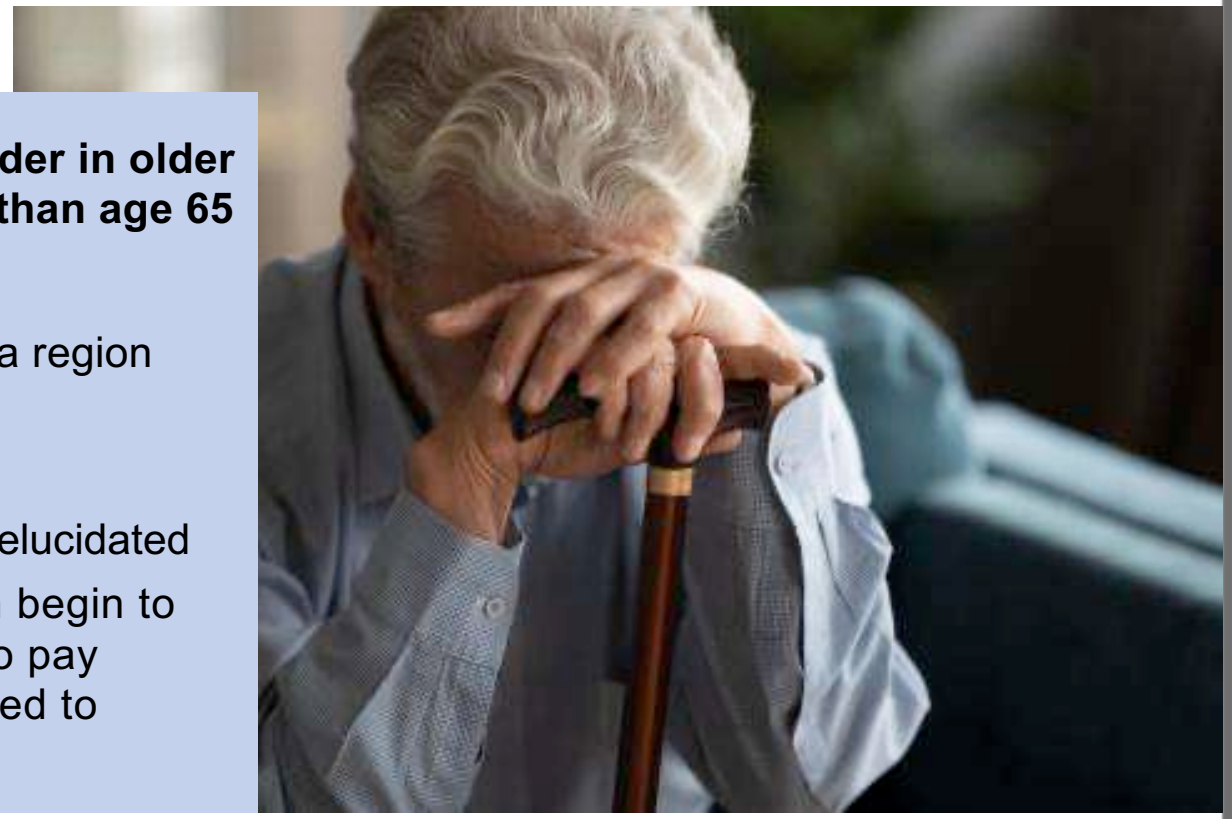
 # Oral liquid solution once daily; Dose restricted to maintain complete blinding

Parkinson's Disease Dementia (PDD)

Up to 80 percent of those with Parkinson's disease eventually experience Parkinson's disease dementia

Parkinson's Disease Dementia

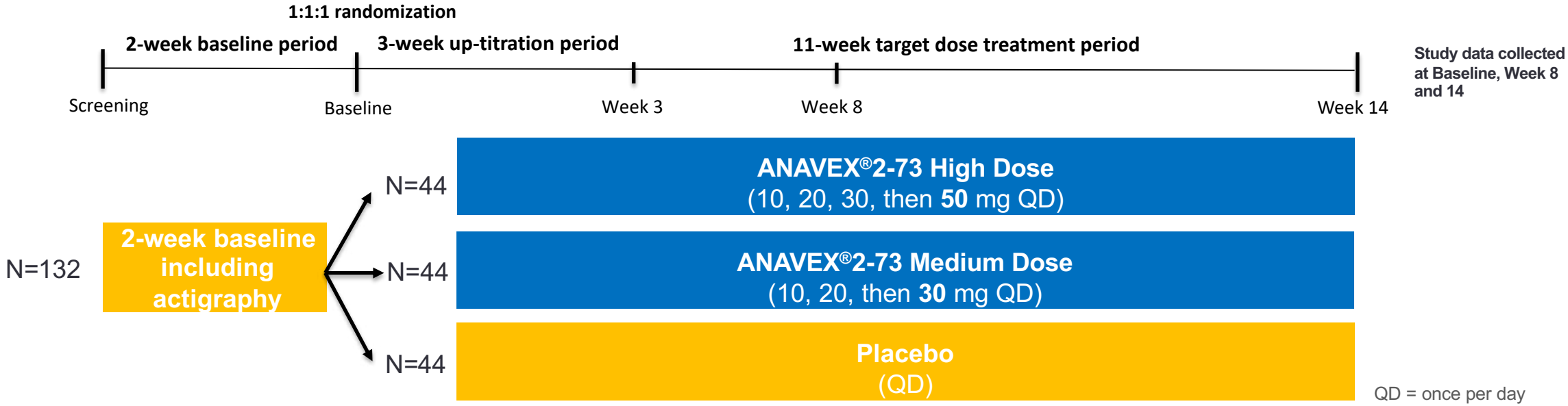
- **Parkinson's disease is a fairly common neurological disorder in older adults, estimated to affect nearly 2 percent of those older than age 65**
  - PD prevalence in US:~1,000,000
  - The brain changes caused by Parkinson's disease begin in a region that plays a key role in movement
  - Highly heterogeneous multisystem disorder
  - Etiology of cognitive impairment in PD has not yet been fully elucidated
  - 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: Aarsland D, Creese B, Politis M, Chaudhuri KR, Ffytche DH, Weintraub D, Ballard C. Cognitive decline in Parkinson disease. Nat Rev Neurol. 2017 Apr;13(4):217-231. doi: 10.1038/nrneurol.2017.27. Epub 2017 Mar 3. PMID: 28257128; PMCID: PMC5643027; www.alz.org/alzheimers-dementia/what-is-dementia/types-of-dementia/parkinson-s-disease-dementia

ANAVEX®2-73 PoC Phase 2 PDD Study Design

A Phase 2 trial to Assess the Safety, Tolerability and Efficacy of ANAVEX®2-73 (*blarcamesine*) Oral Capsules in the Treatment of Parkinson's Disease Dementia

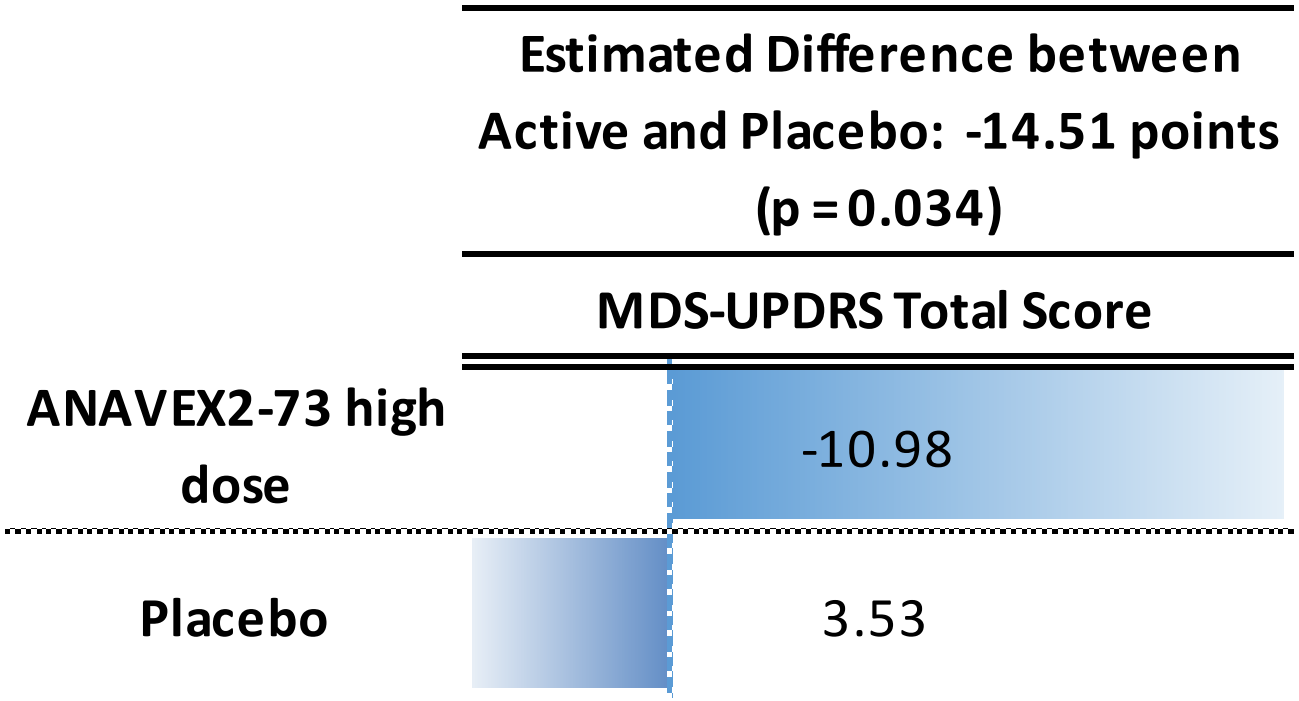


- **PDD Patient Population**
  - Diagnosis of probable Parkinson's disease dementia
  - Diagnosis of idiopathic Parkinson's disease
  - Patients aged ≥ 50 years
  - MoCA score 13-23
- **Key Primary and Secondary Endpoints**
  - Safety and tolerability
  - CDR Cognitive Domain of Attention
  - Sleep function
  - MDS-UPDRS
  - Actigraphy (24-hour monitoring)
  - Entire DNA and RNA sequencing
- **Pre-specified Endpoints**
  - Genetic variants SIGMAR1 (rs1800866),
  - COMT(rs113895332/rs6114320 3) with influence on treatment effect

ANAVEX®2-73-PDD-001 is a Proof of Concept (PoC) Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group, 3-arm, 14-week study

ANAVEX®2-73 Improved MDS-UPDRS Total Score in Placebo-Controlled Parkinson's Disease Dementia Phase 2 Study

MDS-UPDRS Total score -14.51 improvement is clinically relevant and corresponds to a relative improvement of 18.9 % over 14 weeks



- Randomized, double-blind, placebo-controlled Phase 2 trial that randomized 132 patients with Parkinson's disease dementia equally (ratio of 1:1:1) to target doses of 30mg (medium), 50mg (high) ANAVEX®2-73 or placebo

Key Cognitive Domains

Key cognitive features addressed by ANAVEX®2-73 (*blarcamesine*)

The criteria from the National Institute on Aging and Alzheimer's Association (NIA-AA) workgroup mention the following five cognitive domains when diagnosing MCI-AD:

(a) Episodic memory

(b) Attention

(c) Language

(d) Visuospatial skills

(e) Executive functions

Related CDR system domains

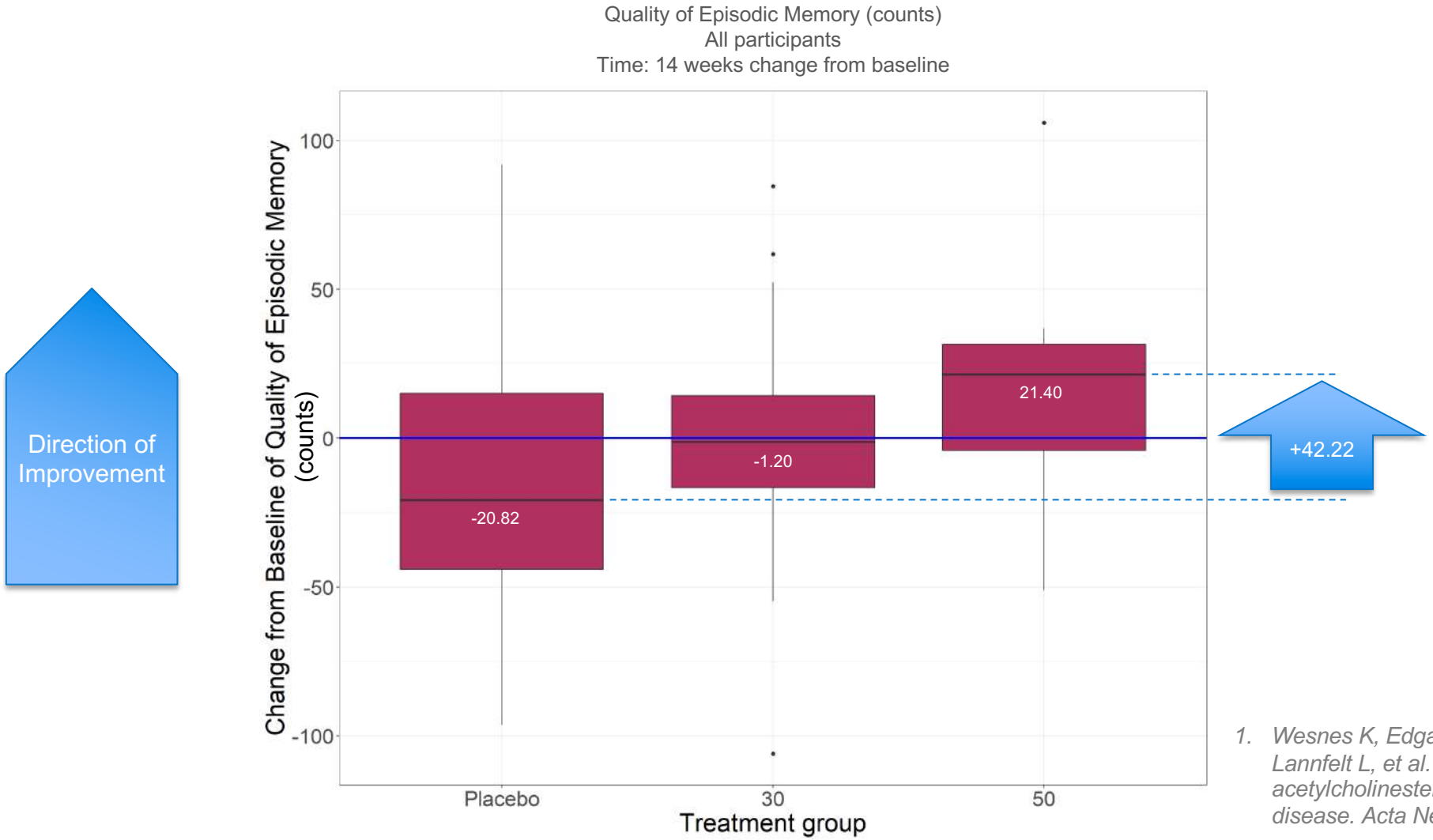
Addressed in PoC Phase 2 PDD Study

Episodic memory	✅
Choice reaction time	✅
Word recognition	✅
Picture recognition	✅
Numeric working memory	✅

Source: Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, Gamst A, Holtzman DM, Jagust WJ, Petersen RC, Snyder PJ, Carrillo MC, Thies B, Phelps CH. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011 May;7(3):270-9. doi: 10.1016/j.jalz.2011.03.008. Epub 2011 Apr 21. PMID: 21514249; PMCID: PMC3312027.

Significant Improvements in Episodic Memory with Increased Dose

ANAVEX®2-73-PDD-001 Study: Dose-dependent, statistically significant improvement of Quality of Episodic Memory with ANAVEX®2-73 (*blarcamesine*)



- A high score reflects ability to store, hold and retrieve information of an episodic nature (e.g., an event or name)
- CDR system Quality of Episodic Memory highly correlated (70%) with ADAS-Cog (r = 0.7)[1]

1. *Wesnes K, Edgar C, Andreasen N, Annas P, Basun H, Lannfelt L, et al. Computerized cognition assessment during acetylcholinesterase inhibitor treatment in Alzheimer's disease. Acta Neurol Scand 2010; 122:270–7*

All participants; ANAVEX2-73 = Active 30 mg, Active 50 mg vs Placebo
J-T test based on actual maintenance dose: p = 0.003

Alzheimer's Disease (AD)

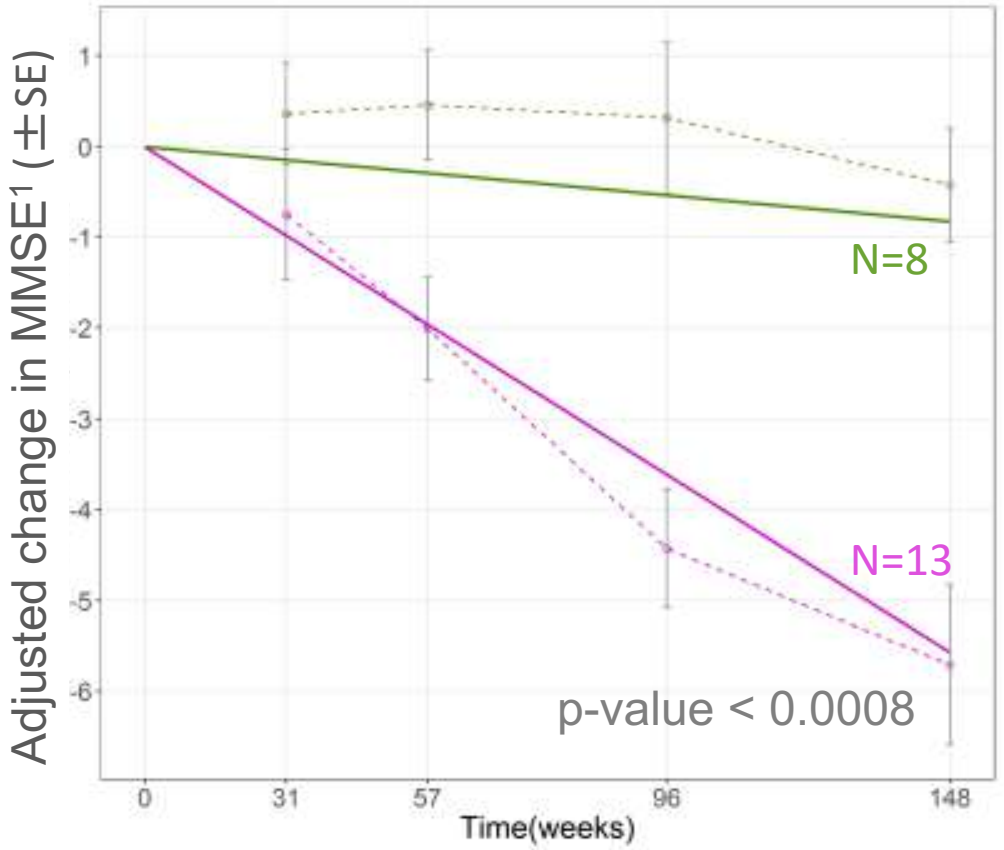
Alzheimer's disease is a progressive, irreversible neurological disease and the most common cause of dementia

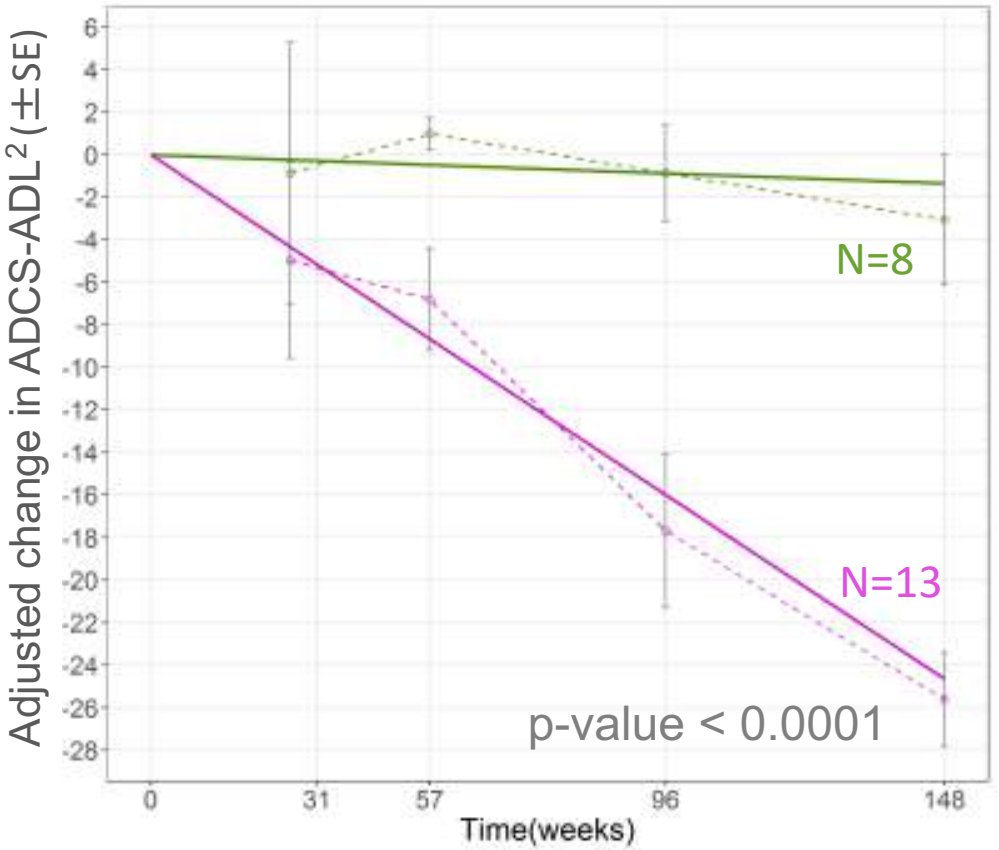
Alzheimer's Disease (AD)

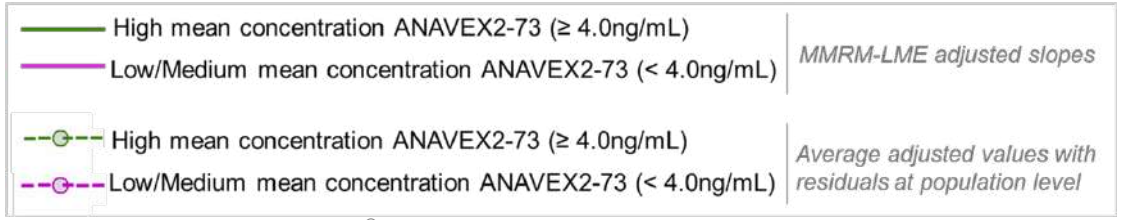
- **Alzheimer's disease incidence highly correlates with age**
  - AD prevalence in US:~5,700,000
  - Estimated 50 million people live with dementia worldwide
  - Today, there are no commercially available therapies to address the underlying cause of Alzheimer's
  - The current annual cost of dementia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

Source: www.alz.org/alzheimers-dementia/what-is-dementia/types-of-dementia/parkinson-s-disease-dementia

ANAVEX®2-73 Demonstrated Improved MMSE[1] and ADCS-ADL[2] Scores in Phase 2a AD Study through 148 Weeks







Dose range 10mg-50mg ANAVEX®2-73 oral once daily.

Source: *Hampel et al. A precision medicine framework using artificial intelligence for the identification and confirmation of genomic biomarkers of response to an Alzheimer's disease therapy: Analysis of the blarcamesine (ANAVEX2-73) Phase 2a clinical study. Alzheimer's Dement. 2020;00:1–14*

[1] *Mini Mental State Examination (MMSE)*

[2] *Alzheimer's Disease Cooperative Study Group - Activities of Daily Living Inventory (ADCS-ADL)*

ANAVEX®2-73 Biomarker Driven Development Strategy in Alzheimer's Disease

Patient Clinical Data

- Cognitive Scores
- Sleep Questionnaires
- Other Scores
- Dose, PK

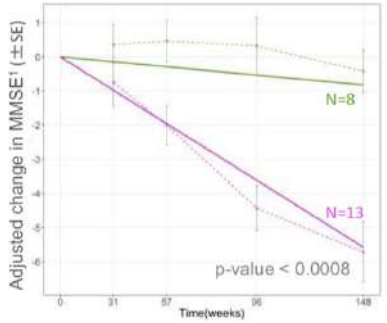
Genomic Data

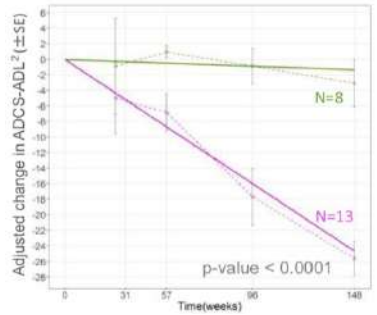
- DNA
- RNA
- Microbiota

Real World Evidence Data (~ 7,000 patients)

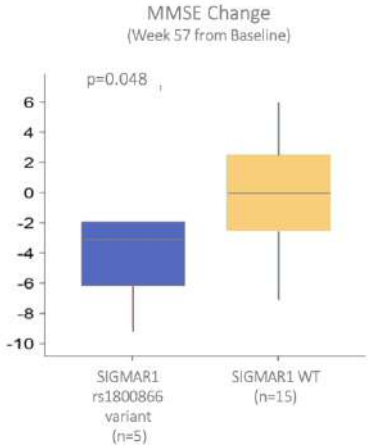
KEM® Integrative AI

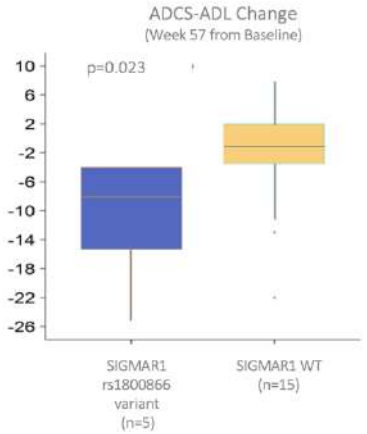
Demonstrated Improved MMSE and ADCS-ADL through 148 weeks for *all* patients





Novel Genomic Biomarkers of Response Identified in Phase 2a AD study -> *Pre*-specified Efficacy Endpoints in *all* ANAVEX®2-73 studies (AD, PDD, RTT)





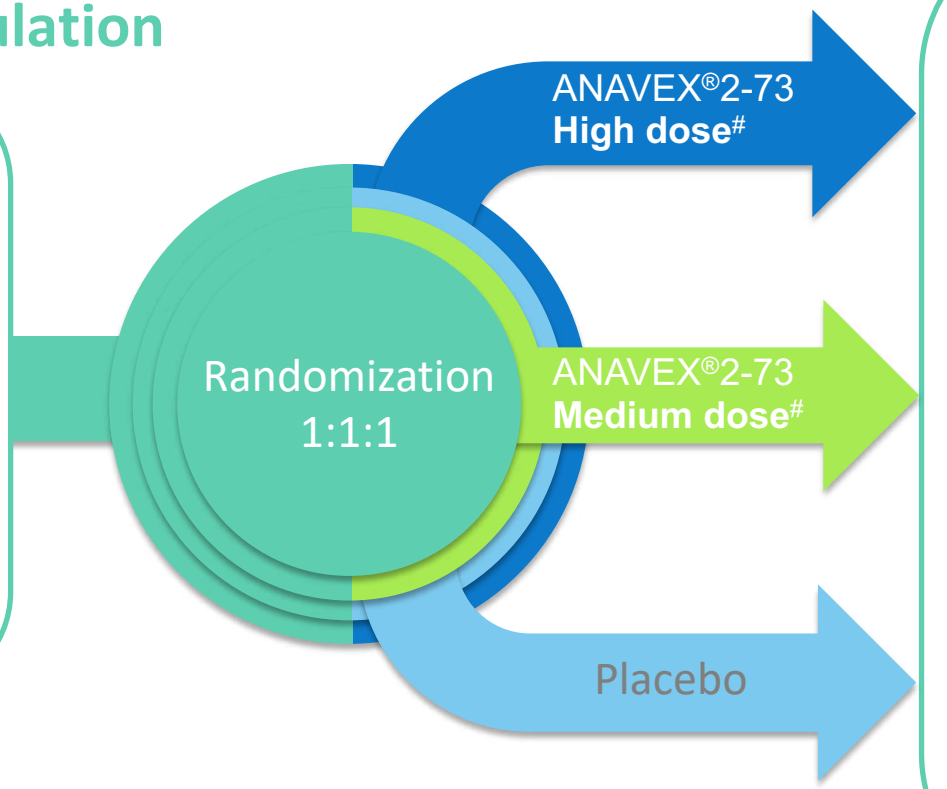
Applied to Phase 2b/3 Alzheimer's disease (AD) study and other indications: Parkinson's disease dementia (PDD) and Rett syndrome (RTT)

ANAVEX®2-73 Phase 2b/3 Alzheimer's Disease and ATTENTION-AD OLE Study

N=509

Early AD patient population

- Confirmed amyloid pathophysiology (CSF/amyloid PET)
- Patients aged 60 to 85 years
- MMSE score 20-28
- Entire DNA and RNA sequencing



48 WEEK STUDY

… and Open Label Extension (OLE) **96 weeks**

ClinicalTrials.gov: NCT03790709

Primary Endpoints
- ADAS-Cog
- ADCS-ADL
- Safety and tolerability

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 Analysis
- Excluding genetic variants SIGMAR1 (rs1800866), COMT (rs113895332/rs61143203) with influence on treatment effect

 # Oral capsule once daily; 50mg (high dose), 30mg (medium dose)

ANAVEX®3-71 Phase 1 Clinical Trial Data

Mechanism of Action (MoA) and Clinical Opportunity:

- Frontotemporal Dementia (FTD)
- Schizophrenias
- Alzheimer’s Disease (AD)

ANAVEX®3-71 Completion and AE Rates Similar to Placebo

Results suggest potentially therapeutic doses of ANAVEX®3-71 can be administered while maintaining a favorable tolerability profile

- The number of TEAEs was equal in each treatment group
- All AEs were mild or moderate in severity and did not lead to any discontinuations

Adverse Events and Safety During the Treatment Period		
	ANAVEX®3-71 (n=16) number (%)	**Placebo (n=14)** number (%)
Patients with any TEAE	10 (62.5%)	8 (57.1%)
Patients with a serious TEAE	0 (0%)	0 (0%)
Patient with a severe TEAE	0 (0%)	0 (0%)
Patients with a TEAE leading to withdrawal	0 (0%)	0 (0%)
AEs ≥ 10%		
Headache	4 (18.2%)	2 (15.4%)
Dizziness	2 (9.1%)	1 (7.7%)
Nasal congestion	2 (9.1%)	1 (7.7%)
Somnolence	0 (0%)	2 (15.4%)

Next steps: Biomarker-driven clinical development dementia program of ANAVEX®3-71 for the treatment of FTD, schizophrenias and Alzheimer's disease

TEAE = treatment-emergent adverse event; AE = adverse event

Anavex is pursuing Large Markets by Applying Precision Medicine Platform 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 platform approach to address the totality of CNS diseases

PRECISION MEDICINE PLATFORM IMPROVES CHANCE OF CLINICAL SUCCESS

Testing for biomarkers demonstrated improved clinical response to ANAVEX®2-73 in Rett syndrome, Parkinson's and Alzheimer's patients correlated with mRNA SIGMAR1 gene expression

NOVEL CNS MECHANISM OF ACTION

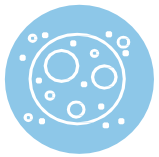
ANAVEX®2-73, an orally available SIGMAR1 agonist, is upstream of neurodevelopment and neurodegeneration and has been shown to restore homeostasis

COMPELLING INITIAL HUMAN DATA

ANAVEX®2-73 Phase 3 and Phase 2 in Rett syndrome, Phase 2 in Parkinson's dementia and Phase 2a trial in Alzheimer's with favorable safety and efficacy through 148 weeks

WORLDWIDE COMMERCIAL RIGHTS AND STRONG IP FOUNDATION

We retain global commercial rights to all of our product candidates and our lead product candidate, ANAVEX®2-73, including patent protection to 2030-2039



SUFFICIENT CASH TO ACHIEVE KEY MILESTONES

Sufficient cash for >5 years to achieve key milestones, including non-dilutive cash from Michael J Fox Foundation, International Rett Syndrome Foundation, Australian government

Anavex Life Sciences Expertise

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Edward R Hammond, MD, MPH, PhD - Chief Medical Officer

Walter E Kaufmann, MD - Chief Scientific Officer

Emmanuel O Fadiran, RPh, PhD - SVP of Regulatory Affairs

Daniel Klamer, PhD - VP of Business Development & Scientific Strategy

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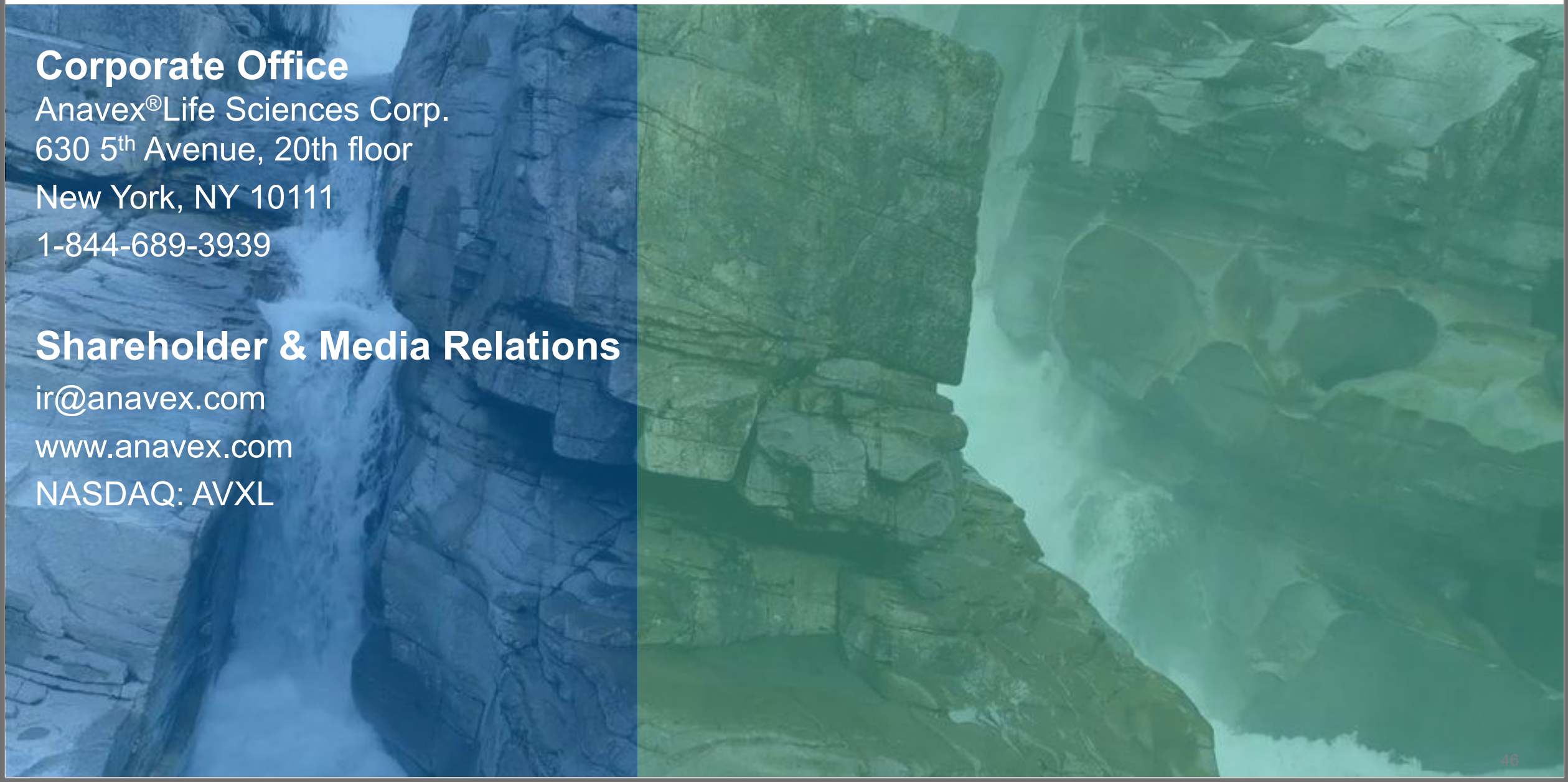

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