At a glance

- Originator Anavex Life Sciences
- Developer ABX-CRO; Anavex Life Sciences
- Class Antidementias; Dimethylamines; Furans; Neuroprotectants; Small molecules
- Mechanism of Action Calcium channel antagonists; Chloride channel modulators; Muscarinic M1 receptor agonists; Muscarinic M2 receptor antagonists; Muscarinic M3 receptor antagonists; NMDA receptor antagonists; Sigma-1 receptor agonists; Sodium channel antagonists; Sodium channel modulators
- Orphan Drug Status
  
  Orphan designation is assigned by a regulatory body to encourage companies to develop drugs for rare diseases.
  
  Yes - Epilepsy; Rett syndrome
- On Fast track
  
  Fast track status is assigned by the US FDA so therapies with the potential to address unmet needs can
move faster through development.

- New Molecular Entity: Yes

**Highest Development Phases**

- Phase II: Alzheimer's disease
- Phase I: Cognition disorders; Epilepsy; Rett syndrome
- Preclinical: Amyotrophic lateral sclerosis; Anxiety disorders; Autistic disorder; Fragile X syndrome; Multiple sclerosis; Parkinson's disease; Stroke

**Most Recent Events**

- 01 Jan 2017: Anavex Life Sciences completes a phase IIa trial for Alzheimer's disease in Australia
- 08 Dec 2016: Updated 12-month efficacy and adverse events data from a phase IIa trial in Alzheimer's disease released by Anavex Life Sciences
- 23 Nov 2016: Updated efficacy and adverse event data from a phase IIa trial in Alzheimer's Disease released by Anavex Life Sciences

**Development Overview**

**Introduction**

Anavex Life Sciences is developing ANAVEX 2-73, a small molecule for the treatment of Alzheimer's disease (AD), epilepsy, stroke, multiple sclerosis and Parkinson's disease. The drug was developed using the company's proprietary SIGMACEPTOR™ platform. Various formulations of the drug have been tested preclinically, but only the oral formulation is being assessed in clinical trials. A phase IIa trial for AD is underway in Australia and a phase Ia single-ascending dose trial of ANAVEX 2-73 in AD was completed and a phase I trial in epilepsy is ongoing in Germany. Phase I development of the candidate is also underway for Rett syndrome and cognition disorders in the US. Preclinical development of the drug for treatment of anxiety, epilepsy including infantile spasms, stroke, Parkinson's disease, Fragile X syndrome, Autism-related disorders, multiple sclerosis and amyotrophic lateral sclerosis is underway in the US.

ANAVEX 2-73 is a tetrahydrofuran derivative that acts as an agonist at M1 muscarinic receptors and intracellular sigma 1 receptors, which are located primarily on the endoplasmic reticulum (ER). It has been shown that the ER stress sensor, IRE1, induces the upregulation of signalling for survival, thereby preventing IRE1 from triggering apoptosis, when cells are under ER stress. ANAVEX 2-73 also exhibits muscarinic cholinergic effects, upregulates Bcl-2, modulates endoplasmic reticulum stress and triggers a series of intracellular effects believed to modify ion channel signalling at the mitochondrial level. It acts as a simultaneous antagonist on presynaptic M2 autoreceptors, and on the presynaptic M3 muscarinic heteroreceptors of the glutamatergic neuronal endings. It is also weakly antagonistic towards NMDA receptors, and at higher doses it acts as an antagonist on sodium and calcium channels. This mixed pharmacodynamic profile suggests that ANAVEX 2-73 may also be an effective anti-amnesic, anti-depressant and neuroprotective drug [1][2][3]. Sigma-1 receptors functionally downregulate certain proteins that play a major role in various pathophysiological conditions including depression, anxiety, epilepsy and brain injury following ischaemic stroke; it has been shown that activating the sigma-1 receptor with agonists can potentially reduce the impact of tau dysfunction [4][5].

In a preclinical study, ANAVEX 2-73 was found to reduce mitochondrial dysfunction and oxidative stress indicating the potential to halt, reverse, decelerate, prevent the course of Alzheimer's disease, in addition to treating the symptoms of disease. Thus, ANAVEX 2-73 may come up as a preventive drug also [6][7]. Anavex conducted another preclinical study that demonstrated marked synergistic activity between ANAVEX 2-73 and donepezil, and on the basis of this finding, is conducting clinical development of the combination product of the two agents [see RDI profile 800039694]. Furthermore, the only metabolite of ANAVEX 2-73, known as ANAVEX 19-144, was being developed as a separate entity [see RDI profile 800027412]. Preclinical and clinical data suggests that ANAVEX 2-73 could be a likely candidate for a precision medicine approach spanning different neurological and psychiatric diseases.

As at July 2016, no recent reports of development had been identified for phase-I development in Alzheimer's-disease (In volunteers) in Germany (PO, Capsule), preclinical development in Alzheimer's-disease (Combination therapy) in France (IV), preclinical development in Alzheimer's-disease (Monotherapy) in Germany (IV).

**Company Agreements**

In October 2016, Anavex Life Sciences entered into a collaboration with Ariana Pharma, to use Ariana’s proprietary KEM® (comprehensive and FDA-tested clinical data analysis system that enables full exploitation
of complex datasets including of smaller numbers of patients) patient stratification technology to potentially accelerate ANAVEX 2-73’s phase II/III Alzheimer’s clinical development [8].

In September 2016, Anavex signed a material transfer agreement with Biogen under which Biogen will test Anavex's ANAVEX 2-73 in an oligodendrocyte precursor cell (OPC) differentiation assay. Results from this assay may lead to an in vivo remyelination study using a demyelination model [9].

In February 2015, Amarantus and Anavex entered into a biomarker service agreement to use Amarantus' proprietary Alzheimer's blood diagnostic LymPro Test® to analyse the pharmacodynamic effect of Anavex 2-73 on the biomarker CD69 expression in specific sub-populations of peripheral blood lymphocytes. Amarantus and Anavex have signed a letter of intent ("LOI"), wherein Amarantus will assist Anavex in planning the scope of the blood-based biomarker components in a phase III study of ANAVEX 2-73 [10].

In August 2010, Anavex signed a definitive master services agreement appointing Genesis BioPharma and ABX-CRO Advanced Pharmaceutical Services as contract research organisations for phase I and phase Ila trials of ANAVEX 2-73. Under the terms of the agreement, Genesis and ABX-CRO gained responsibility for carrying out the clinical trials and regulatory filings for ANAVEX 2-73 [11]. However, as of September 2013, Genesis Biopharma does not appear to be involved in this development.

Key Development Milestones

In July 2014, Anavex reported that it had secured cGMP manufacturing of ANAVEX 2-73 for its clinical trial supplies [12].

Alzheimer's disease (AD) Based on the guidance received from the US FDA, Anavex plans to initiate a double-blind, randomised, placebo-controlled, phase II/III trial of ANAVEX 2-73 for the treatment of Alzheimer’s disease. In October 2016, Anavex Life Sciences entered into a collaboration with Ariana Pharma, to use Ariana's proprietary KEM® (comprehensive and FDA-tested clinical data analysis system that enables full exploitation of complex datasets including of smaller numbers of patients) patient stratification technology to potentially accelerate the phase II/III Alzheimer’s clinical development [8] [13] [14] [15] [16] [17].

In January 2017, Anavex completed a multi-centre two-part phase IIa study that assessed the safety and exploratory efficacy of ANAVEX 2-73 and ANAVEX 2-73/donepezil [8] [36] [37] in patients with mild-moderate AD (ANAVEX2-73-002; NCT02244541). The first part (PART A) was a five-week, randomised, open-label, two-period, cross-over, adaptive trial, whereas the second part (PART B) was an open-label extension for an additional 26 weeks, so as to establish a longer drug effect for the patients who wish to continue on an oral daily dose. The primary endpoint of the adaptive trial was to determine the maximum tolerated dose, safety and tolerability of ANAVEX 2-73. Neuronetrix supported the trial by assessing the cognitive biomarkers in study participants by using its neuro-electrophysiological device, COGNISION™. The crossover, open, prospective, randomised, retrospective trial was initiated in December 2014 and enrolled 32 patients in Australia [17] [18] [19] [20] [21] [22] [23] [24] [25]. In July 2015, positive initial results from the first 12 patients, who completed the PART A of the two-part trial were announced. Based on the initial positive results, Anavex expanded the open-label extension period from 26 weeks to 52 weeks. In December 2015, Anavex released positive safety data and statistically significant improvements on exploratory clinical endpoints from the phase IIa trial in AD. In January 2016, Anavex announced positive dose-response relationship from an interim analysis of the data from the trial [26] [27] [28] [29] [30] [31]. In March 2016, Anavex announced the approval of extension part of the ongoing phase IIa trial by the Ethics Committee in Australia, and initiated the extension study to assess safety and efficacy of ANAVEX 2-73, for additional 104 weeks to enable cumulative safety data gathering over three years, in patients with AD and who completed 52 weeks in part B of the ANAVEX2-73-002 study (ANAVEX2-73-003; NCT02756858). The company also reported detailed dose-response analysis of data from the part A of the trial indicating 14mg of ANAVEX 2-73 to be the required dose to achieve a therapeutic effect and to keep Mini Mental State Examination (MMSE) score unchanged. Anavex released 41-week efficacy and safety data from the study in November 2016 and 57 weeks data in December 2016 [32] [33] [34] [35].

A phase IIa trial of ANAVEX 2-73 in volunteers was completed in Germany in November 2011; the maximum tolerated single dose was defined per protocol as 55-60mg, which was above the equivalent dose shown to have positive effects in mouse models of AD [36] [37]. The randomised, double-blind, placebo-controlled, single ascending dose trial assessed the safety, pharmacodynamics and pharmacokinetics of the orally administered compound in 22 male volunteers. The trial was conducted in collaboration with the clinical research organisation ABX-CRO and the University of Dresden [38] [39] [40] [41]. Full results were presented in November 2014. The product was safe and showed favourable pharmacokinetics profile [42] [43].

The drug combination of ANAVEX 2-73 and donepezil (ANAVEX PLUS) produced up to 80% greater reversal of memory loss in AD models as compared with individual drug treatments [18].

In March 2015, Anavex released positive pharmacodynamics data for ANAVEX 2-73 from preclinical studies in transgenic mouse model of Alzheimer's Disease [44].
Anavex presented preclinical data of the neuroprotective effect of ANAVEX 2-73 and its only metabolite, ANAVEX 19-144, at the International Conference on Alzheimer's Disease and Related Disorders (ICAD-2011) in July 2011 [13][45]. In November 2015, the company released that preclinical studies conducted for the treatment of Alzheimer's disease demonstrated disease modifications against the major Alzheimer's hallmarks in transgenic (3xTg-AD) mice that included cognitive deficits, amyloid and tau pathologies and beneficial effects on neuroinflammation and mitochondrial dysfunctions. Positive preclinical results for ANAVEX 2-73 from studies in animals have been reported wherein administration of ANAVEX 2-73 halted/reversed the course of Alzheimer's disease [46] [47] [48] [2] [49]. Preclinical trials of ANAVEX 2-73 have included oral, IV, ICV and subcutaneous and intraperitoneal dosing [11].

Cognition disorders As of September 2016, ANAVEX 2-73 is being evaluated in a phase I clinical study for the treatment of cognition disorders in neuropsychiatric patients in the US (Anavex pipeline, September 2016).

Epilepsy ANAVEX 2-73 is in phase I clinical development for epilepsy (Anavex pipeline, November 2015). In June 2016, Anavex 2-73 received orphan drug designation from the US FDA for the treatment of infantile spasms [50]. Anavex Life Sciences presented full preclinical results for ANAVEX 2-73 for the treatment of epilepsy in May 2015. The data showed that ANAVEX 2-73 alone and in combination with three generations of epilepsy drugs demonstrated significant improvement in the reduction of seizures in different preclinical models. In three well-established and predictive preclinical anti-seizure models, ANAVEX 2-73 demonstrated positive results with potentially more favourable side effect profile than currently marketed epilepsy drugs [51] [52] [53].

Rett syndrome As of September 2016, ANAVEX 2-73 is being evaluated in a phase I clinical study for the treatment of Rett syndrome in the US and Anavex Life Sciences is planning a phase II study for the treatment of Rett syndrome. The randomised double blind, placebo-controlled study will evaluate safety as the primary endpoint and Rett syndrome conditions including cognitive impairment, motor impairment, behavioural symptoms and seizure activity as the secondary endpoints. Anavex plans to initiate the study in early 2017 [17] [54]. In May 2016, ANAVEX 2-73 received orphan drug designation from the US FDA for the treatment Rett syndrome. Anavex plans a clinical trial to evaluate ANAVEX 2-73 for the treatment of Rett syndrome [55]. In February 2016, Anavex reported preclinical data of ANAVEX 2-73 from an exploratory study in a Rett syndrome mouse model. The data demonstrated dose related and significant improvements in an array of behavioural and gait paradigms in a mouse model with a MECP2-null mutation that causes neurological symptoms that mimic Rett syndrome [56].

Other indications As of September 2016, Anavex is evaluating ANAVEX 2-73 in preclinical studies for the treatment of multiple sclerosis in the US (Anavex pipeline, September 2016). As of June 2016, ANAVEX 2-73 is under preclinical development for fragile X syndrome, autistic disorder and anxiety disorders [57]. In June 2016, the company also released positive preclinical data in a Fragile X preclinical model [58]. Anavex plans to initiate a phase II study of ANAVEX 2-73 in patients with Parkinson's disease [8] [59] [60]. Preclinical studies of ANAVEX 2-73 conducted in convulsive epileptic animal models demonstrated anticonvulsant, anti-amnesic, neuro-protective and anti-depressant properties, indicating its potential to treat additional CNS disorders, including epilepsy and others [18]. ANAVEX 2-73 is in preclinical development for stroke (Anavex pipeline, March 2014).

Anavex Life Sciences, in September 2016, released data from a preclinical study in mice model of Parkinson's disease. The study, which was funded by the Michael J. Fox Foundation for Parkinson's Research, demonstrated that ANAVEX 2-73 was well-tolerated, with no signs of dystonia or stereotypic behaviours, and resulted in significant improvements on behavioral, histopathological, and neuroinflammatory outcome measures. These results were presented at the World Parkinson Congress 2016 [61]. In April 2014, Anavex had stated that a sigma-1 receptor (S1R) agonist demonstrated functional neurorestoration in animal models of Parkinson's disease, which indicates S1R agonists', including ANAVEX 2-73's potential in the disease [5] [62].

In March 2014, Anavex reported that it plans to conduct preclinical studies to evaluate the potential of ANAVEX 2-73 in treatment of amyotrophic lateral sclerosis (ALS) or Lou Gehrig's disease. The decision to initiate preclinical studies in this indication was based on data from other studies that showed efficacy of sigma-1 receptor agonists in suppressing motor neuron damage in ALS animal models [63].

Financial information Anavex announced in January 2017 that Rettsyndrome.org has committed a financial
grant of $US0.6 million which the company will utilise to cover majority of the planned phase II clinical trial of ANAVEX 2-73 in Rett's syndrome [17].

The Michael J. Fox Foundation for Parkinson's Research, in August 2015, awarded a research grant to Anavex, to support the development of ANAVEX 2-73 for the treatment of Parkinson's disease. The grant will fully fund a preclinical study, the data from which is expected to support progress of the drug into clinical development for this indication. The study may also validate the involvement of sigma-1 receptors in disease-modifying therapies targeting Parkinson's disease. The study will be conducted at Lund University in Sweden [30].

In July 2013, Anavex reported that it had closed a round of private placement financing and liability conversion for gross proceeds of $US2.6 million. The company also entered into a common stock purchase agreement with Lincoln Park Capital Fund, whereby the later will initially purchase 250 000 Anavex shares for $US100 000. Anavex may then choose to sell up to a further $US9.9 million to Lincoln Park Capital over a period of three years. Proceeds were to be used to support the clinical development of ANAVEX 27-3 and general corporate purposes [64].

Anavex raised $US1.575 million in July 2011 through the exercise of warrants. The proceeds were to be used to continue the phase I trial of ANAVEX 2-73 and to advance other compounds in the company's pipeline [65].

**Patent Information**

Anavex reported in August 2015 that it had received a notice of allowance from the US Patent and Trademark Office (USPTO) for patent application number 14/205 637 related to ANAVEX 2-73. The allowed patent claims cover formulations and treatments that provide particular coverage relating to improved sigma receptor ligands and their use. The patent upon issuance will provide protection until at least 2035. The company expects that the patent to be issued by the end of 2015. Further, the company reported that it had applied for additional patent application for ANAVEX 2-73, covering compositions and therapies [66].

**Drug Properties & Chemical Synopsis**

- **Route of administration**: IV, PO
- **Formulation**: Capsule, unspecified
- **Class**: Antidementias, Dimethylamines, Furans, Neuroprotectants, Small molecules
- **Mechanism of Action**: Calcium channel antagonists; Chloride channel modulators; Muscarinic M1 receptor agonists; Muscarinic M2 receptor antagonists; Muscarinic M3 receptor antagonists; NMDA receptor antagonists; Sigma-1 receptor agonists; Sodium channel antagonists; Sodium channel modulators
- **WHO ATC code**
  - N03A (Antiepileptics)
  - N04 (Anti-Parkinson Drugs)
  - N05A (Antipsychotics)
  - N05B (Anxiolytics)
  - N06D (Anti-Dementia Drugs)
  - N07 (Other Nervous System Drugs)
  - N07X (Other Nervous System Drugs)
  - N07X-X (Other nervous system drugs)
- **EPhMRA code**
  - N3A (Anti-Epileptics)
  - N4 (Anti-Parkinson Drugs)
  - N5A (Antipsychotics)
  - N7 (Other CNS Drugs)
  - N7D (Anti-Alzheimer Products)
  - N7X (All other CNS drugs)
Table of Contents

- At a glance
- Development Overview
  - Introduction
  - Company agreements
  - Key development milestones
  - Patent information
- Drug Properties & Chemical Synopsis
- Trial Landscape
  - Summary Table
  - Orphan Status
- Commercial Information
  - Involved Organisations
- Scientific Summary
  - Pharmacokinetics
  - Adverse events
  - Pharmacodynamics
  - Therapeutic trials
- Development History
- References

Trial Landscape

<table>
<thead>
<tr>
<th>Indication</th>
<th>Phase 0</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Phase IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unspecified</td>
<td></td>
<td>-</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alzheimer's disease</td>
<td></td>
<td>1</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Rett syndrome</td>
<td></td>
<td>-</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Development Status

Summary Table

Download Data (CSV)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Patient Segment</th>
<th>Phase</th>
<th>Countries</th>
<th>Route / Formulation</th>
<th>Developers</th>
<th>Event Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's disease</td>
<td>-</td>
<td>Phase II</td>
<td>Australia</td>
<td>IV / unspecified</td>
<td>Anavex Life Sciences</td>
<td>01 Dec 2014</td>
</tr>
<tr>
<td>Alzheimer's disease</td>
<td>-</td>
<td>Phase II</td>
<td>Australia</td>
<td>PO / Capsule</td>
<td>Anavex Life Sciences</td>
<td>01 Dec 2014</td>
</tr>
<tr>
<td>Alzheimer's disease</td>
<td>In volunteers</td>
<td>No development reported (I)</td>
<td>Germany</td>
<td>PO / Capsule</td>
<td>Anavex Life Sciences</td>
<td>16 Jul 2016</td>
</tr>
<tr>
<td>Alzheimer's disease</td>
<td>Monotherapy</td>
<td>No development reported (Preclinical)</td>
<td>Germany</td>
<td>IV / unspecified</td>
<td>Anavex Life Sciences</td>
<td>16 Jul 2016</td>
</tr>
<tr>
<td>Alzheimer's disease</td>
<td>Combination therapy With donepezil</td>
<td>No development reported (Preclinical)</td>
<td>France</td>
<td>IV / unspecified</td>
<td>Anavex Life Sciences</td>
<td>16 Jul 2016</td>
</tr>
<tr>
<td>Amyotrophic lateral sclerosis</td>
<td>-</td>
<td>Preclinical</td>
<td>USA</td>
<td>unspecified / unspecified</td>
<td>Anavex Life Sciences</td>
<td>01 Apr 2014</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>-</td>
<td>Preclinical</td>
<td>USA</td>
<td>PO / unspecified</td>
<td>Anavex Life Sciences</td>
<td>28 Jun 2016</td>
</tr>
</tbody>
</table>
Autistic disorder - Preclinical USA PO / unspecified Anavex Life Sciences 28 Jun 2016
Cognition disorders
In neuropsychiatric - Phase I USA unspecified / unspecified Anavex Life Sciences 07 Sep 2016
Epilepsy - Phase I Germany unspecified / unspecified Anavex Life Sciences 03 Nov 2015
Fragile X syndrome - Preclinical USA PO / unspecified Anavex Life Sciences 28 Jun 2016
Multiple sclerosis - Preclinical USA unspecified / unspecified Anavex Life Sciences 07 Sep 2016
Parkinson's disease - Preclinical USA unspecified / unspecified Anavex Life Sciences 01 Apr 2014
Rett syndrome - Phase I USA unspecified / unspecified Anavex Life Sciences 07 Sep 2016
Stroke - Preclinical Germany unspecified / unspecified Anavex Life Sciences 13 Mar 2014

Orphan Status

<table>
<thead>
<tr>
<th>Indication</th>
<th>Patient Segment</th>
<th>Country</th>
<th>Organisation</th>
<th>Event Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td></td>
<td>USA</td>
<td>Anavex Life Sciences</td>
<td>22 Jun 2016</td>
</tr>
<tr>
<td>Rett syndrome</td>
<td></td>
<td>USA</td>
<td>Anavex Life Sciences</td>
<td>18 May 2016</td>
</tr>
</tbody>
</table>

Commercial Information

Involved Organisations

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Involvement</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anavex Life Sciences</td>
<td>Originator</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Anavex Life Sciences</td>
<td>Owner</td>
<td>Switzerland</td>
</tr>
<tr>
<td>The Michael J. Fox Foundation for Parkinson's Research</td>
<td>Funder</td>
<td>USA</td>
</tr>
<tr>
<td>Rettsyndrome.org</td>
<td>Funder</td>
<td>USA</td>
</tr>
<tr>
<td>Lund University</td>
<td>Collaborator</td>
<td>Sweden</td>
</tr>
<tr>
<td>ABX-CRO</td>
<td>Collaborator</td>
<td>Germany</td>
</tr>
<tr>
<td>Amarantus Bioscience Holdings</td>
<td>Collaborator</td>
<td>USA</td>
</tr>
<tr>
<td>Ariana Pharmaceuticals</td>
<td>Collaborator</td>
<td>France</td>
</tr>
</tbody>
</table>

Scientific Summary

Pharmacokinetics

Pharmacokinetics data from a phase I trial in 22 healthy male volunteers showed that AVANEX 2-73 was suitable for daily oral dosing. There were dose-proportional increases in the Cmax and AUC values for both AVANEX 2-73 and its main metabolite. The t½ value for AVANEX 2-73 was 8.56h and 28.74h for its metabolite [42].

Adverse Events

Treatment with oral ANAVEX 2 73 daily dose between 10mg and 50mg was well tolerated, without clinically significant treatment-related adverse events and serious adverse events in patients with mild-to-moderate Alzheimer’s disease, at 57 weeks in a phase IIa trial. As reported earlier, no patients discontinued treatment due to adverse events and the safety profile was consistent with that observed in a phase I trial. The two-part phase IIa study enrolled 32 patients [67] [32] [14] [31].

The maximum tolerated dose of ANAVEX 2-73 in a single ascending dose phase Ia trial in volunteers was defined per protocol as 55-60mg, which was above the equivalent dose shown to have positive effects in mouse models of AD. No significant changes in laboratory or electrocardiogram (ECG) parameters were
observed. ANAVEX 2-73 was well tolerated below the 55-60mg dose level, with only mild adverse events observed in some volunteers. Adverse events to occur at doses above the maximum tolerated dose included headache and dizziness, which were moderate in severity and reversible. The randomised, double-blind, placebo-controlled trial was conducted in 22 male volunteers. There were no serious adverse events reported and no study discontinuations due to adverse events. No dose-limiting adverse events or laboratory abnormalities were noted at doses of 1, 10, 30, 40 or 50mg. Maximum tolerated dose was defined as 55mg as per protocol. No dose-dependent or time-dependent changes in ECG were observed [42] [36].

In preclinical trials (both the forced (Porsolt) swim test and the open-field test), ANAVEX 2-73 demonstrated anti-depressant effects with no signs of sedation. In the chimney test, ANAVEX 2-73 showed no statistically significant motor impairment within the effective dose range [52].

Pharmacodynamics

Summary

**Preclinical studies:** Once-daily oral ANAVEX 2-73, significantly decreased the amyloid toxicity and induced strong reversal of memory loss after one month and two months treatment, respectively, in Tg2576 transgenic mouse model of Alzheimer's Disease, in which the sigma-1 receptor (S1R) expression was impaired through S1R KO (knock out). Additionally, the drug also led to significant improvement in the expression of reactive oxygen species (ROS) as well as plasticity related IEG and transcription factors in the mouse hippocampus [44].

ANAVEX 2-73 administered once-daily for 2 months significantly improved spatial working memory and long-term spatial reference memory in Tg2576 mice. In these preclinical studies, spatial working memory was assessed by spontaneous alternation in a Y-maze, and long-term spatial reference memory was assessed by place learning in a water maze. Additionally, treatment with ANAVEX 2-73 reduced expression of oxidative stress markers, and increased expression of functional and synaptic plasticity markers in the brain of Tg2576 mice [47].

ANAVEX 2-73 effectively restored mitochondrial functionality, and prevented oxidative stress and apoptosis following mitochondrial disfunction caused by injection of oligomeric Aβ25-35 peptide in mice (a nontransgenic Alzheimer's disease model) [69].

ANAVEX 2-73 (0.1, 0.3 mg/kg, IP) blocked amyloid β25-35 peptide-induced memory deficits and liquid peroxidation in the hippocampus, in mouse models of Alzheimer's disease. The drug also showed a synergistic effect when administered in combination with donepezil, but no effect was seen in combination with memantine [70]. ANAVEX 2-73 failed to affect learning abilities alone, but dose-dependently reversed the learning deficits induced by the M1 muscarinic antagonist scopolamine, the NMDA receptor antagonist dizocilpine, or the central injection of amyloid β25-35 peptide, a non-transgenic model of Alzheimer's disease. These effects were blocked by a pre-injection of the sigma-1 receptor antagonist BD 1047, confirming an action at muscarinic and sigma-1 receptor sites. These effects were examined in several models of pharmacological and pathological amnesia in mice submitted to a short-term and long-term memory test, spontaneous alternation and passive avoidance, respectively. Since muscarinic agonists and sigma-1 receptor agonists are potent neuroprotective drugs against amyloid toxicity, the neuroprotective effects of AVEX 2-73 were examined in amyloid β25-35 peptide-treated mice. ANAVEX 2-73 was injected once, 20 minutes before amyloid β25-35 peptide and 7 days before the behavioral tests and biochemical analyses. Injection of scrambled amyloid β peptide was used as control. ANAVEX 2-73 dose-dependently prevented the appearance of amyloid β25-35 peptide-induced learning deficits, at 300-1000 µg/kg, the same dose-range as observed for acute anti-amnesic effects. ANAVEX 2-73 prevented the amyloid β25-35 peptide-induced increase in lipid peroxidation and caspase-3 expression in the CA1 pyramidal layer of the hippocampus [72].

Both ANAVEX 2-73 and its active metabolite ANAVEX 19-144 improved neurotoxicity and cognition deficits associated with Alzheimer's disease in animal models [71].

ANAVEX 2-73 exhibited significant anticonvulsive dose-dependent action by providing almost complete protection from tonic seizures. In maximum electroshock (MES)-induced convulsions, ANAVEX 2-73 30 mg/kg alone provided 90% protection. ANAVEX 2-73 demonstrated significant anticonvulsive dose-dependent activity and provided almost complete protection from tonic seizures. ANAVEX 2-73 demonstrated a significant synergistic effect with three generations of epilepsy drugs for the reduction of seizures. In MES-induced convulsions, ANAVEX 2-73 10 mg/kg in combination with ethosuximide 200 mg/kg provided 80% protection, while no protection was observed at the same dose of ethosuximide alone. In the pentylentetrazole-induced convulsion model, ANAVEX 2-73 metabolite 10 mg/kg in combination with valproic acid (VPA) showed 92% protection from tonic seizures, compared with 12.5% protection at the same dose of VPA alone. This combination also prolonged life during a seizure, compared to when VPA was used alone. ANAVEX 2-73 metabolite 5 mg/kg in combination with gabapentin 100 mg/kg resulted in 90% protection from tonic seizures as compared with 40% protection with same dose of gabapentin alone in the
Preclinical studies of ANAVEX 2-73 demonstrated a significant reduction in number of spasms. In an infant rat model with infantile spasms, following prenatal priming with betamethasone in infant rats, spasms were recorded for 90 minutes following postnatal trigger of spasms with NMDA injection. Treatment with ANAVEX 2-73 exhibited a significant reduction in number of spasms by 55% compared with vehicle (p = 0.0002) [68].

In a Fragile X preclinical model, ANAVEX 2-73 significantly improved all behaviours tested and reversed hyperactivity and impairment in learning and memory (p = 0.0001) [58].

In a 6-hydroxydopamine lesions mouse model of Parkinson’s disease, ANAVEX 2-73, daily for five weeks, resulted in significant motor recovery (p<0.05), neurohistological restoration (p<0.05) and reduced microglial activation (p<0.05) [61].

**Therapeutic Trials**

Administration of oral ANAVEX 2 73 in patients with mild-to-moderate Alzheimer's disease in a phase IIa trial demonstrated a calculated treatment benefit of 1.8 points on the MMSE scale (p < 0.016) and a calculated treatment benefit of 4 points on the ADCS-ADL score (p < 0.019), at 57 weeks. There were continued significant improvements of cognitive, functional and behavioral scores from baseline in a group of patients, despite non-optimised dosing of ANAVEX 2 73 throughout the 12-month trial. Interim results from the trial showed a stabilisation of cognitive and functional measures at 41 week in Alzheimer’s patients treated with oral dose of ANAVEX 2 73. A continued stabilisation of both cognitive (MMSE) and functional (ADCS-ADL) measures in patients treated with ANAVEX 2-73 was observed. A positive correlation was also observed with all measured scores (MMSE, ADCS-ADL, Cogstate, HAM-D and electroencephalographic activity and event-related potentials (EEG/ERP) at both 57 weeks and 41 weeks. Earlier, interim results from the trial demonstrated that ANAVEX 2 73 improved psychomotor function, and had statistically significant improvements in attention (p < 0.05) and working memory (p < 0.001) with clinically important magnitude. ANAVEX2 73 further demonstrated cognitive improvement across all doses in all exploratory cognitive measurements, including the Cogstate battery and P300 tests, which consistently demonstrated improvements from baseline in the completed part A portion of the study in 32 mild-to-moderate Alzheimer’s patients. Statistically significant improvements in the biomarker event-related potentials (ERP) was observed at week 5 of the treatment (p < 0.0007). The two-part phase Ila study will enrol 32 patients with mild-to-moderate Alzheimer’s disease The detailed dose-response analysis of the data indicated that low-high dose was statistically significant to affect MMSE-Δ and ERP-Δ scores with MMSE-Δ (p=0.0285) and ERP-Δ (p=0.0168), respectively. However, no notable difference between ANAVEX 2-73 alone and in combination with donepezil were observed [67] [32] [33] [34] [26] [27] [31] [25].

**Development History**

<table>
<thead>
<tr>
<th>Event Date</th>
<th>Update Type</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Jan 2017</td>
<td>Trial Update</td>
<td>Anavex Life Sciences completes a phase Ila trial for Alzheimer's disease in Australia [17] Updated 03 Feb 2017</td>
</tr>
<tr>
<td>08 Dec 2016</td>
<td>Scientific Update</td>
<td>Updated 12-month efficacy and adverse events data from a phase Ila trial in Alzheimer’s disease released by Anavex Life Sciences [67] Updated 26 Dec 2016</td>
</tr>
<tr>
<td>23 Nov 2016</td>
<td>Scientific Update</td>
<td>Updated efficacy and adverse event data from a phase Ila trial in Alzheimer's Disease released by Anavex Life Sciences [32] Updated 29 Nov 2016</td>
</tr>
<tr>
<td>05 Oct 2016</td>
<td>Trial Update</td>
<td>Anavex Life Sciences plans a phase II trial for an Parkinson’s disease in USA [8] Updated 11 Feb 2016</td>
</tr>
<tr>
<td>22 Sep 2016</td>
<td>Scientific Update</td>
<td>Pharmacodynamics data from a preclinical study in Parkinson's disease released by Anavex Life Sciences [61] Updated 26 Sep 2016</td>
</tr>
<tr>
<td>Date</td>
<td>Event</td>
<td>Details</td>
</tr>
<tr>
<td>------------</td>
<td>------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>07 Sep 2016</td>
<td>Phase Change - I</td>
<td>Phase-I clinical trials in Cognition disorders in USA before September 2016 (Anavex Life Sciences pipeline, September 2016) Updated 07 Sep 2016</td>
</tr>
<tr>
<td>07 Sep 2016</td>
<td>Phase Change - I</td>
<td>Phase-I clinical trials in Rett syndrome in USA before September 2016 (Anavex pipeline, September 2016) Updated 07 Sep 2016</td>
</tr>
<tr>
<td>07 Sep 2016</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical trials in Multiple sclerosis in USA before September 2016 (Anavex Life Sciences pipeline, September 2016) Updated 07 Sep 2016</td>
</tr>
<tr>
<td>07 Sep 2016</td>
<td>Trial Update</td>
<td>Anavex plans a phase II trial for Rett syndrome in USA (Anavex pipeline, September 2016) Updated 07 Sep 2016</td>
</tr>
<tr>
<td>27 Jul 2016</td>
<td>Scientific Update</td>
<td>Additional efficacy data from a phase Ila trial in Alzheimer's disease released by Anavex Life Sciences [33] Updated 01 Aug 2016</td>
</tr>
<tr>
<td>16 Jul 2016</td>
<td>Phase Change - No development reported</td>
<td>No recent reports of development identified for phase-I development in Alzheimer's disease (In volunteers) in Germany (PO, Capsule) Updated 16 Jul 2016</td>
</tr>
<tr>
<td>16 Jul 2016</td>
<td>Phase Change - No development reported</td>
<td>No recent reports of development identified for preclinical development in Alzheimer's disease (Combination therapy) in France (IV) Updated 16 Jul 2016</td>
</tr>
<tr>
<td>16 Jul 2016</td>
<td>Phase Change - No development reported</td>
<td>No recent reports of development identified for preclinical development in Alzheimer's disease (Monotherapy) in Germany (IV) Updated 16 Jul 2016</td>
</tr>
<tr>
<td>28 Jun 2016</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical trials in Anxiety disorders, Fragile X syndrome and Autistic disorders in USA before June 2016 (PO) [57] Updated 28 Jun 2016</td>
</tr>
<tr>
<td>06 Jun 2016</td>
<td>Scientific Update</td>
<td>Preclinical data from a in Fragile X syndrome released by Anavex Life Sciences [58] Updated 17 Aug 2016</td>
</tr>
<tr>
<td>20 May 2016</td>
<td>Trial Update</td>
<td>Anavex Life Sciences plans a clinical trial for Rette syndrome in USA [55] Updated 24 May 2016</td>
</tr>
<tr>
<td>18 May 2016</td>
<td>Scientific Update</td>
<td>Pharmacodynamics data from preclinical studies in Epilepsy released by Anavex Life Sciences [68] Updated 20 May 2016</td>
</tr>
<tr>
<td>10 Mar 2016</td>
<td>Scientific Update</td>
<td>Additional efficacy data from a phase Ila trial in Alzheimer's disease released by Anavex [34] Updated 15 Mar 2016</td>
</tr>
<tr>
<td>01 Mar 2016</td>
<td>Trial Update</td>
<td>Anavex Life Sciences initiates a phase II extension trial for Alzheimer's disease in Australia (PO) (NCT02756858) Updated 05 May 2016</td>
</tr>
<tr>
<td>25 Feb 2016</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical trials in Rett syndrome in USA (unspecific route), before February 2016 Updated 01 Mar 2016</td>
</tr>
<tr>
<td>11 Jan 2016</td>
<td>Scientific Update</td>
<td>Updated efficacy data from a phase Ila trial in Alzheimer's disease released by Anavex [26] Updated 14 Jan 2016</td>
</tr>
<tr>
<td>09 Nov 2015</td>
<td>Scientific Update</td>
<td>Interim efficacy data from a phase Ila trial in Alzheimer's disease released by Anavex [27] Updated 05 Jan 2016</td>
</tr>
<tr>
<td>Date</td>
<td>Type</td>
<td>Description</td>
</tr>
<tr>
<td>------------</td>
<td>-----------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>03 Nov 2015</td>
<td>Phase Change - Phase I</td>
<td>Phase-I clinical trials in Epilepsy in Germany (unspecified route) (Anavex pipeline, November 2015)</td>
</tr>
<tr>
<td>28 Sep 2015</td>
<td>Trial Update</td>
<td>Anavex Life Sciences completes enrolment in its phase IIa trial for Alzheimer's disease in Australia (NCT02244541)</td>
</tr>
<tr>
<td>22 Jul 2015</td>
<td>Scientific Update</td>
<td>Initial efficacy and adverse events data from a phase IIa trial in Alzheimer's disease released by Anavex Life Sciences [31]</td>
</tr>
<tr>
<td>15 May 2015</td>
<td>Scientific Update</td>
<td>Pharmacodynamics data from preclinical studies in Epilepsy released by Anavex Life Sciences [52]</td>
</tr>
<tr>
<td>18 Feb 2015</td>
<td>Trial Update</td>
<td>Anavex plans a phase III trial for Alzheimer's disease in USA [10]</td>
</tr>
<tr>
<td>09 Feb 2015</td>
<td>Scientific Update</td>
<td>Pharmacodynamics data from preclinical studies in Epilepsy released by Anavex Life Sciences [53]</td>
</tr>
<tr>
<td>01 Dec 2014</td>
<td>Phase Change - II</td>
<td>Phase-II clinical trials in Alzheimer's disease in Australia (IV)</td>
</tr>
<tr>
<td>01 Dec 2014</td>
<td>Phase Change - II</td>
<td>Phase-II clinical trials in Alzheimer's disease in Australia (PO)</td>
</tr>
<tr>
<td>01 Apr 2014</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical trials in Amyotrophic lateral sclerosis in USA (unspecified route)</td>
</tr>
<tr>
<td>01 Apr 2014</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical trials in Parkinson's disease in USA (unspecified route)</td>
</tr>
<tr>
<td>13 Mar 2014</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical development for Stroke in Germany (unspecified route)</td>
</tr>
<tr>
<td>13 Mar 2014</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical development for Epilepsy in Germany (unspecified route)</td>
</tr>
<tr>
<td>10 Mar 2014</td>
<td>Trial Update</td>
<td>Anavex Life Sciences plans preclinical studies for Amyotrophic lateral sclerosis in USA [63]</td>
</tr>
<tr>
<td>06 Nov 2012</td>
<td>Scientific Update</td>
<td>Pharmacodynamics data from a preclinical study in Alzheimer's disease released by Anavex Life Sciences [69]</td>
</tr>
<tr>
<td>Date</td>
<td>Event Type</td>
<td>Description</td>
</tr>
<tr>
<td>------------</td>
<td>-------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>14 Nov 2011</td>
<td>Scientific Update</td>
<td>Adverse events data from a phase I trial in Alzheimer's disease (In volunteers) released by Anavex [36] Updated 15 Nov 2011</td>
</tr>
<tr>
<td>14 Nov 2011</td>
<td>Trial Update</td>
<td>Anavex completes a phase I trial in Alzheimer's disease (In volunteers) in Germany Updated 15 Nov 2011</td>
</tr>
<tr>
<td>16 Mar 2011</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical trials in Stroke in Germany (unspecified route) Updated 16 Mar 2011</td>
</tr>
<tr>
<td>15 Mar 2011</td>
<td>Phase Change - Preclinical</td>
<td>Phase-I clinical trials in Alzheimer's disease (in volunteers) in Germany (PO) Updated 16 Mar 2011</td>
</tr>
<tr>
<td>22 Dec 2010</td>
<td>Scientific Update</td>
<td>Pharmacodynamics data from a preclinical trial in Alzheimer's disease released by Anavex [71] Updated 20 Jul 2012</td>
</tr>
<tr>
<td>21 Dec 2010</td>
<td>Regulatory Status</td>
<td>Anavex Life Sciences files a regulatory application with BfArM in Germany for permission to conduct clinical trials in Alzheimer's disease [71] Updated 16 Mar 2011</td>
</tr>
<tr>
<td>02 Sep 2008</td>
<td>Trial Update</td>
<td>Anavex completes preclinical trials of ANAVEX 2-73 in Alzheimer's disease Updated 20 Jul 2012</td>
</tr>
<tr>
<td>19 Nov 2007</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical trials in Alzheimer's disease in Germany (Parenteral) Updated 16 Mar 2011</td>
</tr>
<tr>
<td>19 Nov 2007</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical trials in Alzheimer's disease in Germany (PO) Updated 16 Mar 2011</td>
</tr>
<tr>
<td>19 Nov 2007</td>
<td>Phase Change - Preclinical</td>
<td>Preclinical trials in Epilepsy in Germany (unspecified route) Updated 16 Mar 2011</td>
</tr>
</tbody>
</table>

**References**

1. Anavex Encouraged by New Sigma-1 Receptor Study That May Explain Therapeutic Efficacy of ANAVEX 2-73 for Alzheimer's Disease.
   [Media Release](#)

2. ANAVEX advances drug candidates for treatment of epilepsy.
   [Media Release](#)

   [Media Release](#)

4. Anavex Encouraged by Data Showing Sigma-1 Receptor Reduces Tau Dysfunction, a Hallmark of Alzheimer's Disease.
   [Media Release](#)

5. Anavex Reports Fiscal Third Quarter 2014 Financial Results.
   [Media Release](#)
   Media Release
7. Anavex to Present at SeeThruEquity Investor Conference in New York City.
   Media Release
8. Anavex Life Sciences and Ariana Pharma Collaborate to Accelerate Timelines and Improve Efficiency of Alzheimers and Parkinsons Clinical Development Programs.
   Media Release
9. Anavex Compound to be Tested in Biogen Neurological Protection Model.
   Media Release
10. Amarantus Announces First Alzheimer's Biomarker Services Collaboration for LymPro Test(Rm) With Anavex Life Sciences Corp.
    Media Release
11. Anavex appoints contract research organizations to initiate Phase I/IIa clinical programs, regulatory strategies in Alzheimer's disease.
    Media Release
12. Anavex Achieves Key Milestone as it Secures cGMP Manufacturing for Drug Candidate Trial Supplies.
    Media Release
13. Anavex and Ariana Pharma Collaborate to Accelerate Timelines and Improve Efficiency of Alzheimer's and Parkinson's Clinical Development Programs.
    Media Release
    Media Release
15. Anavex Announces Preparation of Regulatory Filings Based on Guidance From the FDA.
    Media Release
    ctiprofile
17. Anavex Life Sciences Receives Grant From Rettsyndrome.org to Commence U.S. Phase 2 Trial in 2017.
    Media Release
18. Anavex to Present Initial Clinical Data From the Phase 2a Clinical Trial of ANAVEX 2-73 at the Alzheimers Association International Conference (AAIC).
    Media Release
    Media Release
    Media Release
21. Anavex Begins Enrollment of Alzheimer's Patients in Phase 2a Clinical Trial of ANAVEX 2-73 and ANAVEX PLUS.
    Media Release
22. Neuronetrix has been selected by Anavex Life Sciences Corp. to support the upcoming Phase 2a clinical trial for ANAVEX 2-73.
23. Anavex Receives Regulatory Approval to Initiate Phase 2a Clinical Trial of ANAVEX 2-73 and ANAVEX PLUS for Alzheimer's Disease.


25. Phase IIa Study of ANAVEX2-73 Adaptive-Trial-Design With Repeated Doses, MTD Finding, Pharmacodynamic and Bioavailability Evaluation in Patients With Mild to Moderate Alzheimer's Disease With a 6-Month Open Label Follow-Up Period


27. Positive Safety Data, Statistically Significant Improvements on Exploratory Clinical Endpoints.

28. DUE DILIGENCE REPORT: Anavex Life Sciences Completes Enrollment for Clinical Phase 2a - BrokerBank Securities.

29. Anavex Completes Patient Enrollment for Phase 2a Alzheimers Trial Ahead of Schedule.

30. Anavex Awarded Grant From The Michael J. Fox Foundation for Parkinsons Research.

31. Anavex Presents Positive Initial Phase 2a Study Data With ANAVEX 2-73 Showing Early Evidence of Improving Cognition in Patients With Alzheimers Disease at AAIC 2015.

32. Anavex Life Sciences Announces Data on 41-Week Treatment of ANAVEX 2-73 for Patients with Alzheimers Disease Investigational Treatment suggests to curb Cognitive and Functional Decline.

33. Anavex Presents 31-Week Efficacy Data from Phase 2a Study of ANAVEX 2-73 in Alzheimers Patients at AAIC 2016.

34. Anavex Announces Two-Year Clinical Extension Study of ANAVEX 2-73 and Presents Phase 2a Dose-Response Analysis at AAT Conference.

35. An Extension Study of ANAVEX2-73 in Patients With Mild to Moderate Alzheimer's Disease

36. Anavex successfully completes a Phase 1 clinical trial for ANAVEX 2-73.

37. Anavex to present corporate update at BIO CEO & Investor Conference.

38. ANAVEX: FIRST-IN-HUMAN DOSING COMMENCED IN ANAVEX 2-73 CLINICAL TRIAL FOR ALZHEIMER'S DISEASE.
39. ANAVEX SCREENING HEALTHY VOLUNTEERS FOR PHASE I, FIRST-IN-HUMAN CLINICAL STUDY IN ALZHEIMER'S DISEASE.

40. ANAVEX RECEIVES APPROVAL TO COMMENCE PHASE I CLINICAL TRIAL IN ALZHEIMER'S DISEASE.

41. A Phase 1 Dose Escalation Study to Investigate Safety, Tolerability, and Pharmacokinetics of ANAVEX 2-73 in Healthy Male Subjects

42. Anavex Announces Positive Phase 1 Data for ANAVEX 2-73, Lead Candidate for the Treatment of Alzheimer's.

43. Anavex to Present Full Phase 1 Clinical Trial Data for ANAVEX 2-73 at CNS Summit 2014 Conference.

44. Anavex Presents Positive Results for Both ANAVEX 2-73 and ANAVEX 3-71 in Alzheimer's Models at 2015 AD/PD(Tm) Conference.

45. Anavex presents data on neuroprotective evidence for ANAVEX 2-73, lead compound for Alzheimer's disease.


47. Anavex Announces Positive Data for ANAVEX 2-73 in Alzheimer's Disease.


49. Anavex reports animal study results as lead Alzheimer's disease compound approaches phase 1 clinical trials.


52. Anavex Releases Promising Full Preclinical Epilepsy Data at Antiepileptic Drug Trials XIII Conference.

53. Anavex Confirms Positive Preclinical Epilepsy Data for ANAVEX 2-73 - Validation as Potential Platform Drug for Multiple Neurodegenerative Diseases.

54. A randomised, double-blind, placebo controlled phase II study of ANAVEX 2-73 in patients with Rett
   Media Release

56. Anavex Presents Preclinical Results of ANAVEX 2-73 in Rett Syndrome.
   Media Release

57. Anavex to Present at the 2016 Rett Syndrome Symposium.
   Media Release

58. Anavex Reports Fiscal Third Quarter 2016 Financial Results.
   Media Release

59. Anavex Reports Fiscal First Quarter 2016 Financial Results.
   Media Release

60. A phase 2 trial of ANAVEX 2-73 in a non-disclosed indication
   ctiprofile

   Media Release

62. Anavex Encouraged by Scientific Data Confirming Sigma-1 Receptor Agonist is Potentially Disease-Modifying in Parkinson's Disease.
   Media Release

63. Anavex Encouraged By Scientific Data Confirming Sigma-1 Receptor Agonist Extends Survival in ALS (Lou Gehrig's Disease).
   Media Release

64. Anavex raises $2.6-million in private placement and conversion of liabilities, enters into $10-million financing commitment and appoints CEO.
   Media Release

65. Anavex raises $1.575 million.
   Media Release

   Media Release

67. Anavex Life Sciences Announces 12-Month Data of ANAVEX 2-73 in a Phase 2a Study in Mild-to-Moderate Alzheimers Disease Patients.
   Media Release

68. Anavex Announces Positive Preclinical Data for ANAVEX 2-73 in Infantile Spasms.
   Media Release

69. ANAVEX 2-73 shown to block oxidative stress, preventing onset of Alzheimer's disease.
   Media Release

70. Anavex presents compelling data at world's largest Alzheimer's conference.
   Media Release
71. Anavex files Phase I regulatory submission for ANAVEX 2-73 in Alzheimer's disease.

Media Release


Available from: URL: http://www.sfn.org