Junaxo

Dr Patrick Howson
CEO, Junaxo Inc.

JNX1001 – A novel neurotrophic factor modulator in development for ALS

Apr 7th 2016

NEUROTECH
INVESTING & PARTNERING

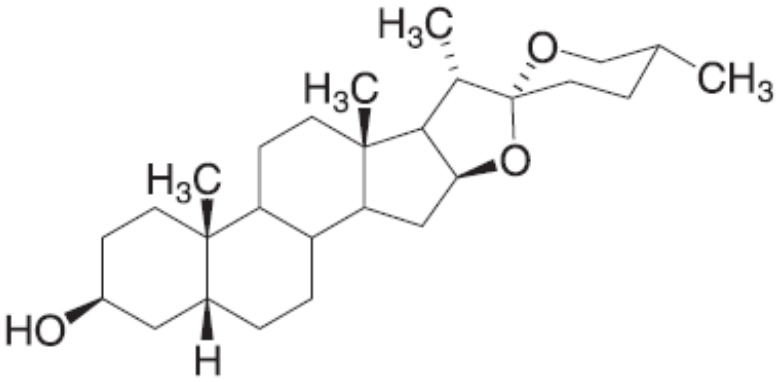
Junaxo Inc.

- Focussed on neurodegenerative disorders
- Develop compounds through Proof-of-Concept studies
- Several Orphan Disease indications
- Multiple licensing opportunities

Product	Indication	2016	2017	2018	2019
JNX1001	ALS	Biomarker studies	Phase II proof-of-concept clinical trials		
JNX3001	Parkinson's Disease	In vivo PoC	Phase I and II clinical trials		
JNX3001	ALS	Preclinical evaluation		Phase II PoC trial	
JNX4001	Dyskinesia	Preclinical evaluation		Phase II PoC trial	

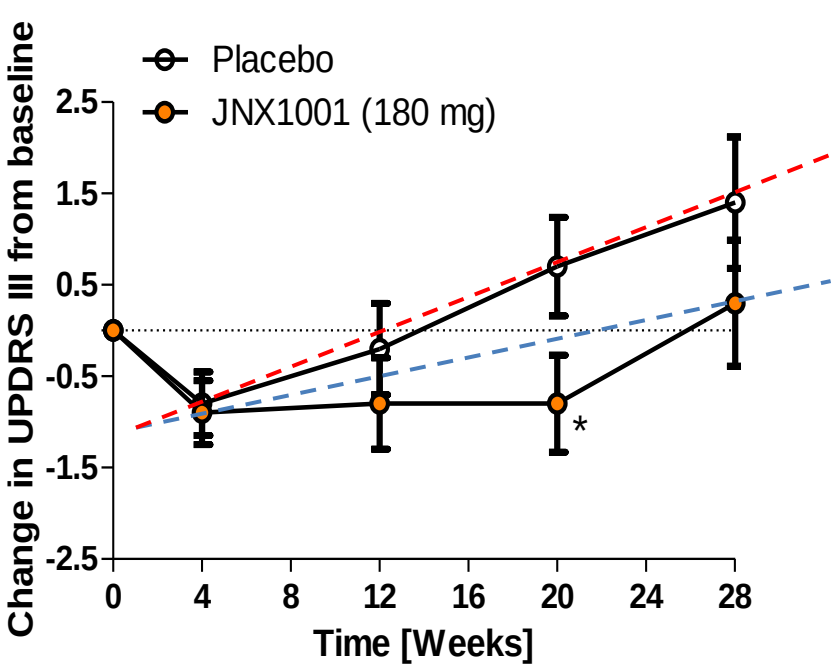
JNX1001 - a small molecule drug with potential to stimulate endogenous neurotrophic factor actions

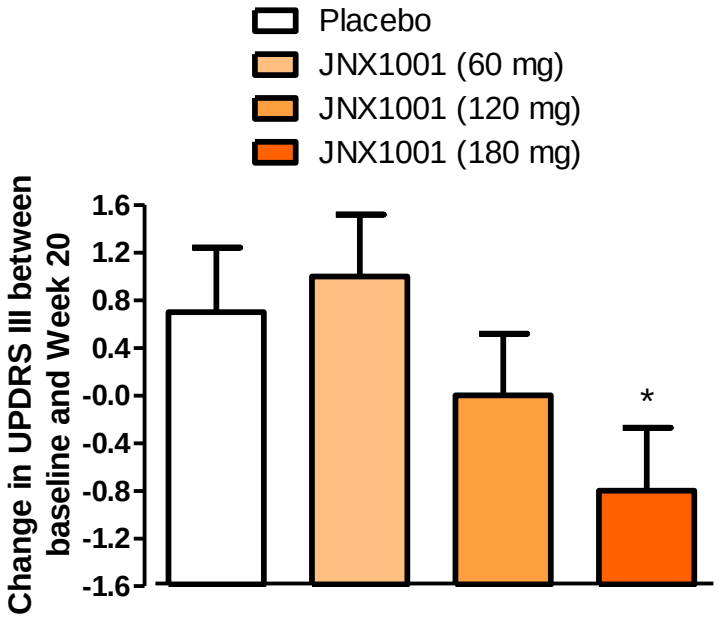
JNX1001



- Synthetic, small molecule chemical entity
- Increases GDNF and BDNF synthesis
- Neuroprotective in a range of neuronal cell types
- Orally active, for once daily dosing
- Toxicology and safety pharmacology studies completed
- Phase I and II studies performed – good emerging safety profile
  - 28 weeks dosing in man performed in a Phase II study in PD

Phase II clinical study in Parkinson's disease





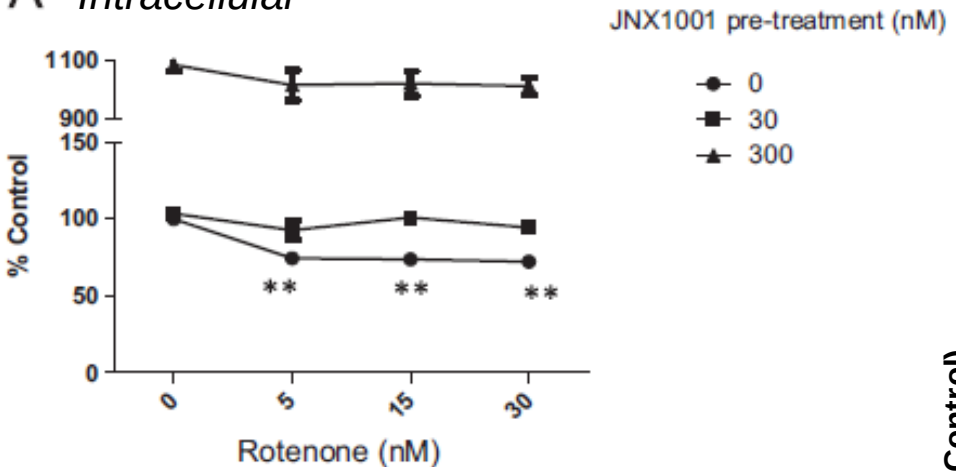
- High dose slowed the rate of decline in motor symptoms by >50%
- Dose dependent effect on motor symptoms
- Junaxo acquired JNX1001 and repurposed for ALS

If JNX1001 slows disease progression by >50% in ALS it will be a breakthrough drug

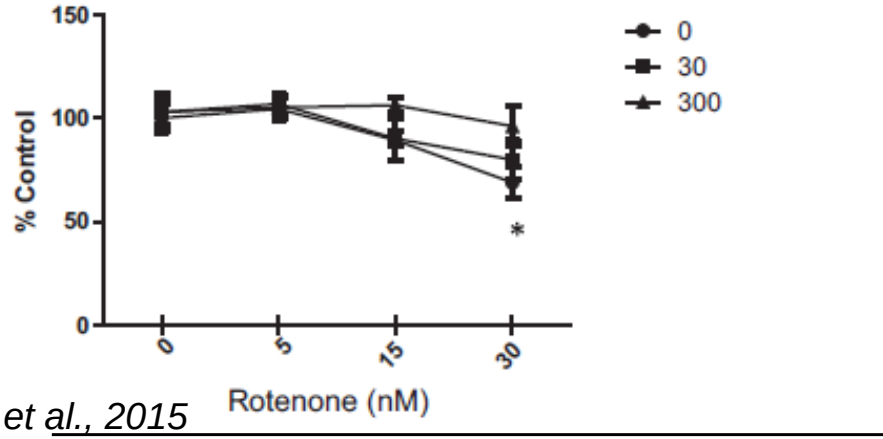
Neurotrophic factor inducing effects

Cultured SH-SY5Y cells

A *Intracellular*

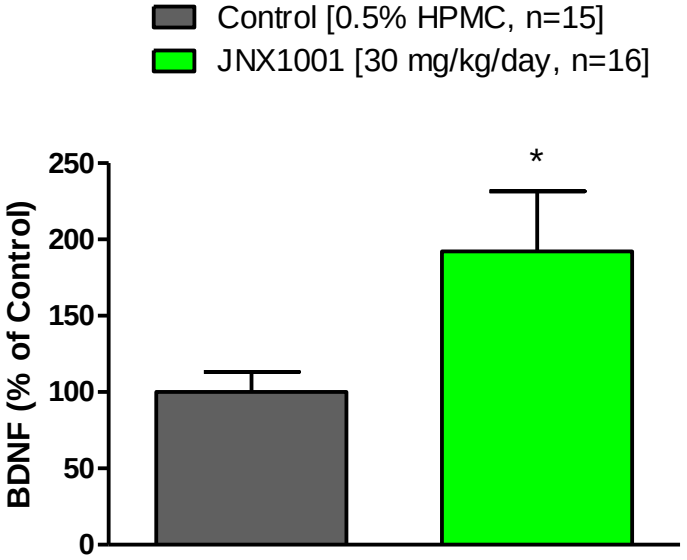


B *Extracellular*



Kim et al., 2015

CNS tissue from mSOD1G93A mice



Similar effects seen on GDNF

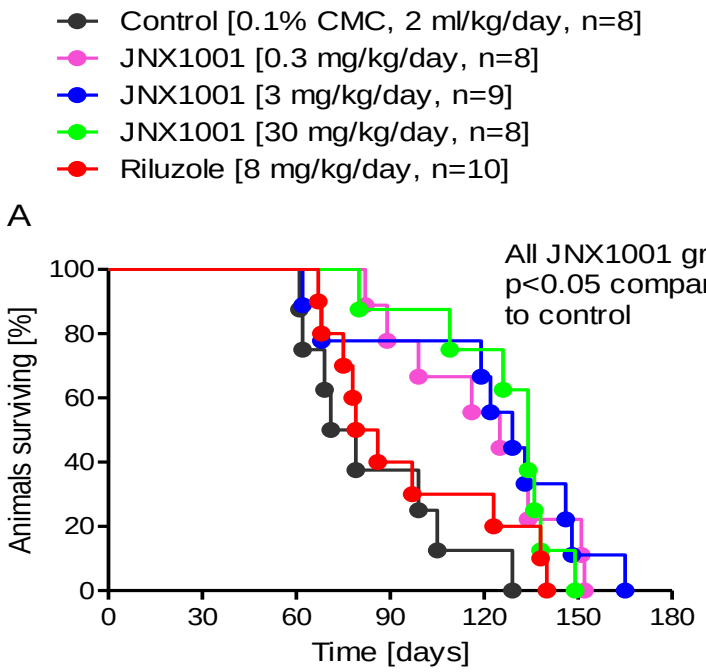
JNX1001 in mSOD1 mice

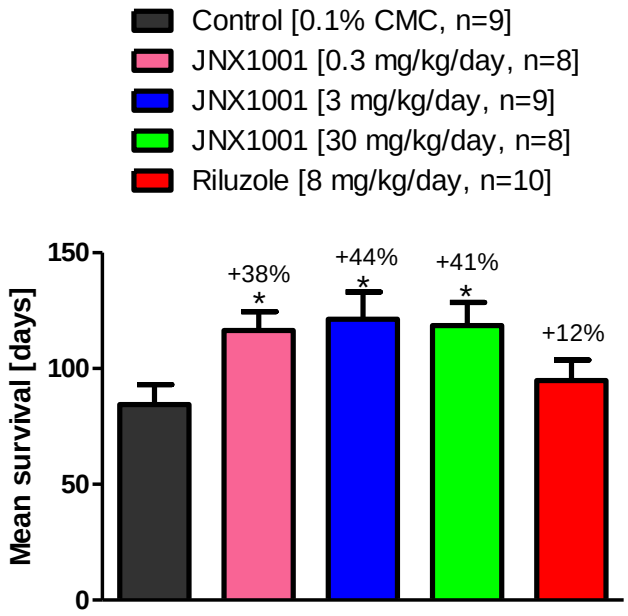
- Two studies performed in different laboratories using mSOD1^{G93A} mice (gold-standard pre-clinical ALS model)

- Study 1: Survival study
  - Mice administered JNX1001 from day 60 until death or unable to feed themselves
  - Survival, motor performance and CMAP characteristics examined

- Study 2: Effect on motor neuron study
  - Mice administered JNX1001 for 50 days starting on day 70
  - Muscle force, contraction characteristics, muscle phenotype, motor unit survival and motor neuron survival examined

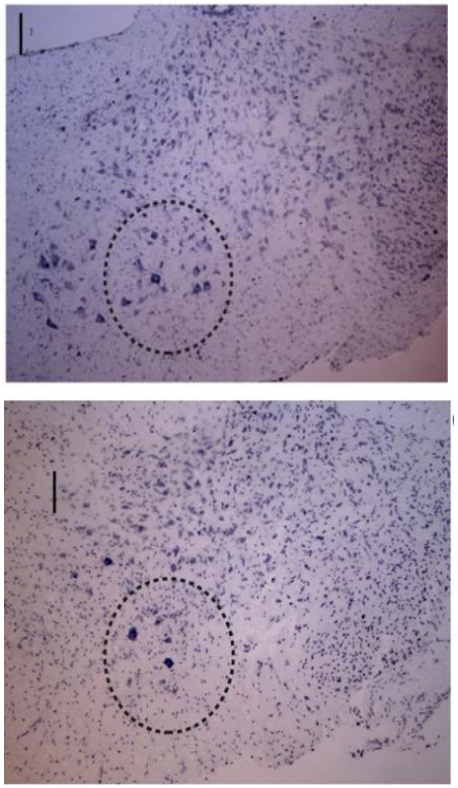
Study 1: JNX1001 increases survival and maintains motor performance

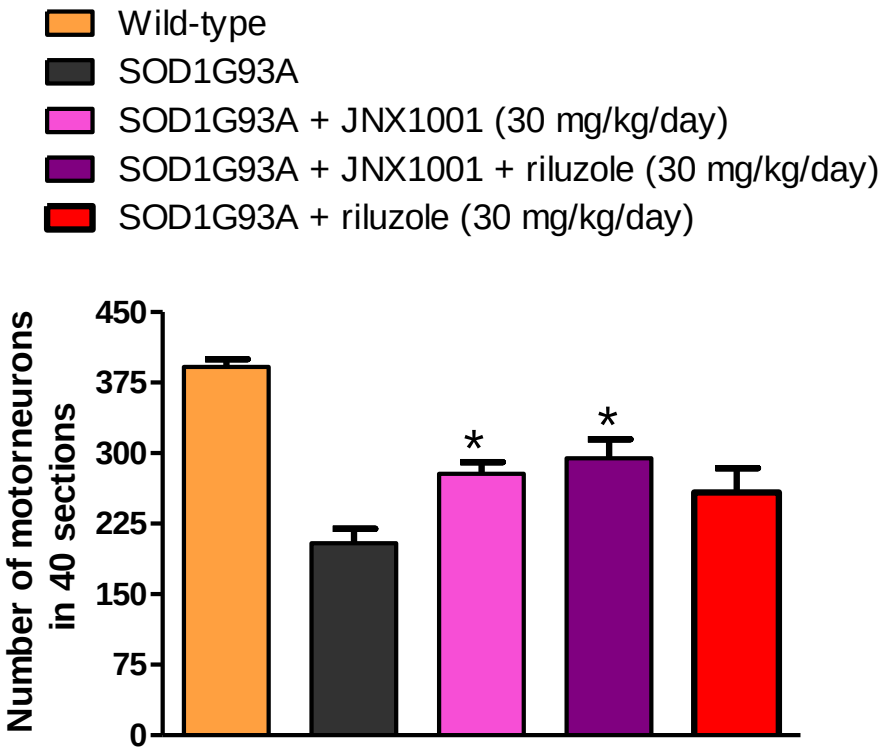




Group	Rotarod test (s)	Grid test (no. of stumbles)	Hanging test (s)	CMAP amplitude (mV)	Survival time (days)
Control [0.1% CMC]	31.6 ± 5.8	23.6 ± 1.1	50.8 ± 1.8	6.3 ± 1.1	84.4 ± 8.6
JNX1001 [0.3 mg/kg/day]	70.0 ± 6.9****	14.7 ± 1.2****	44.5 ± 1.9***	12.9 ± 1.2****	116.4 ± 8.2*
JNX1001 [3 mg/kg/day]	66.0 ± 6.7****	15.0 ± 1.2****	42.3 ± 2.1****	14.9 ± 1.3****	121.3 ± 11.7*
JNX1001 [30 mg/kg/day]	64.2 ± 6.9****	15.5 ± 1.4****	42.4 ± 2.2****	12.9 ± 1.2**	118.6 ± 9.9*
Riluzole [8 mg/kg/day]	42.7 ± 5.8	21.2 ± 1.1	46.3 ± 1.9*	9.6 ± 1.2**	94.8 ± 8.9

Study 2: JNX1001 reduces loss of spinal motor neurons





- JNX1001 significantly reduced motor neuron loss
  - JNX1001 also significantly increased the number of motor units and improved muscle functionality

Efficacy observed in additional models of motor neuron damage

- Genetic mutations in SOD1 only account for a small fraction of all ALS cases.
  - Important to show that the efficacy of JNX1001 is not restricted to models of SOD1 impairment.
- JNX1001 is efficacious in non-SOD1 mediated models of ALS:
  - BSSG - a toxin thought to be the cause of Guam type ALS-PDC.
  - Progressive motor neuropathy in *pmn* mice, model of SMA, possibly due to microtubule dysfunction
  - Sciatic nerve crush mice

Pharmacology demonstrated across a range of ALS-relevant models

Next stages of development

- Extensive development package already available
  - Open IND for ALS
  - Orphan disease designation in ALS in US and EU
  - GMP manufacturing complete
  - Early clinical studies complete

- Preclinical studies – Ongoing (2016 – 2017)
  - mSOD1G93A mouse study
  - Demonstrate efficacy and define peripheral biomarker of drug effect
  - Define variability of biomarkers in patient-derived tissue

- Phase II PoC clinical trial (2018 – 2020)
  - Randomised, placebo-controlled double-blind study
    - 52 weeks, approx. 80 subjects randomised 1:1 (placebo:JNX1001)
  - Demonstration of target engagement/ drug effect
  - Preliminary efficacy investigated using rate of decline in ALSFRS-R

Licensing opportunity

- Multiple licensing opportunities for JNX1001