Pioneering the next frontier of genetic medicines with artificial intelligence.

VERGE genomics

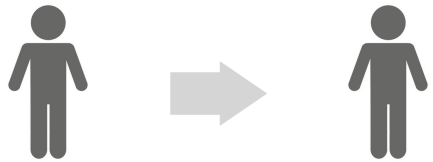
WHY NOW

Human genetics have made new therapies possible.

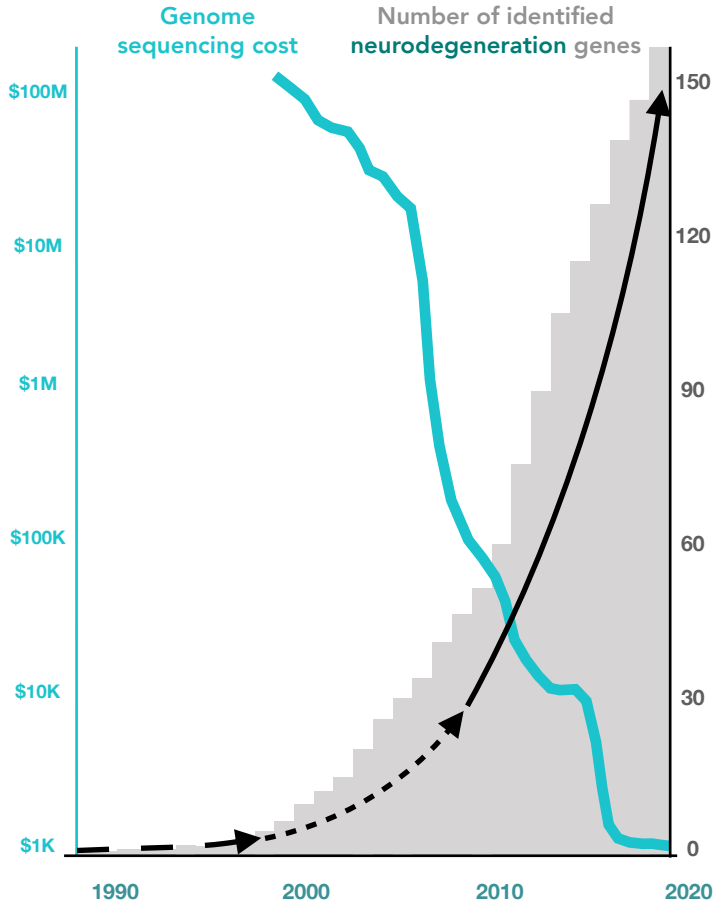
Oncology in 1990s = Neuroscience in 2010s

Traditional approach:
Animal —> human

New approach:
Human —> human



Human validated targets +
biomarkers is key to clinical success



2016

Spinraza® approved
First ever drug for spinal muscular atrophy (SMA)

2017

Exondys 51® approved
First ever drug for Duchenne muscular dystrophy (DMD)

2018

2019

Zolgensma® approved
For SMA

Vyondys 53® approved
For DMD

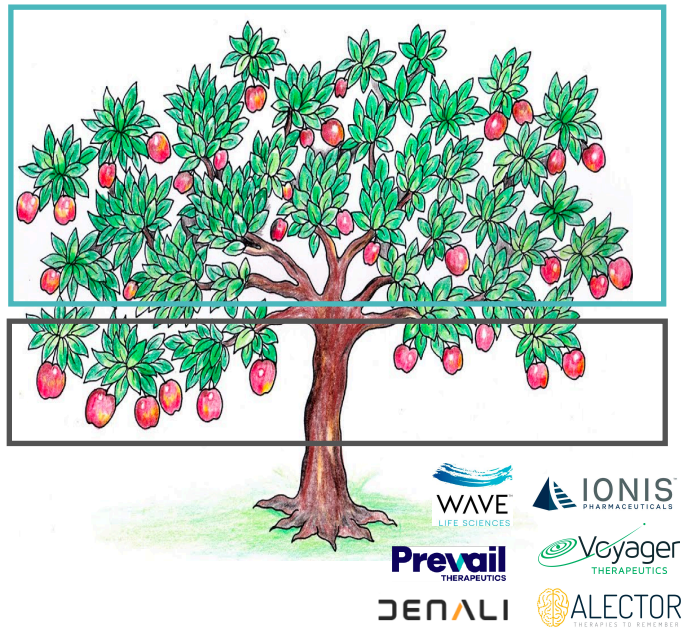
2020

Evrysdi® approved
For SMA

Viltepso® approved
For DMD

PROBLEM

Current genetic therapies treat a small fraction of patients.



The Next Frontier: Genetic Pathway Therapies

Verge is developing targeted therapies that functionally correct genetic pathways

Greater commercial viability

Increased scope of patients addressable with genetic therapies

Product differentiation

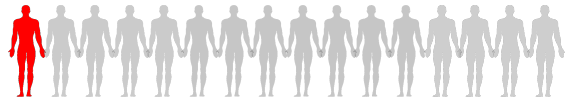
Multiple first-in-class product opportunities

Multiple modalities

Diversified small molecule and genetic therapy opportunities

Low Hanging Fruit: Genetic Therapies

Targeted therapies are limited to correction of rare genetic mutations



Limited commercial potential

Few treatable patients, limited to rare genetic mutations

Competitive, saturated space

Intense competition for few targets

Limited modalities

Often limited to gene therapies that face tox and delivery challenges

SOLUTION

Verge's all-in-human platform extends the power of human genetics to larger markets.

Human Genetics

We begin with well-validated genetic targets where mutations directly cause disease in humans.

Targets from human genetics **increase the probability of clinical efficacy.**

Human Tissue

Using our industry-leading transcriptomics database with > 6500 proprietary patient brain samples, we find disease pathways linking these genetic targets and ways to functionally counteract genetic shortfalls.

Therapeutics targeting shared genetic pathways are likely to be **effective across larger patient populations.**

Human Validation

We confirm disease efficacy of human-derived targets in neurons derived directly from patients.

Patient-derived neurons enable the selection of candidates with **disease modifying potential.**

Genetically Defined POC

We demonstrate clinical proof of concept in a monogenic patient population with mutations in the core genetic target.

Beginning with a homogenous population **increases the probability of success** and provides a beachhead into larger populations.

LEAD PROGRAM

VG001: Amyotrophic Lateral Sclerosis

ALS is a rapidly progressing disease caused by the death of motor neurons, resulting in paralysis + respiratory failure.

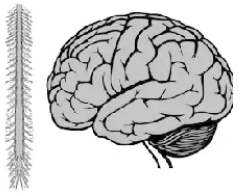
Most patients die within three years of first noticing symptoms.

There are currently no drugs that meaningfully slow or stop the disease.

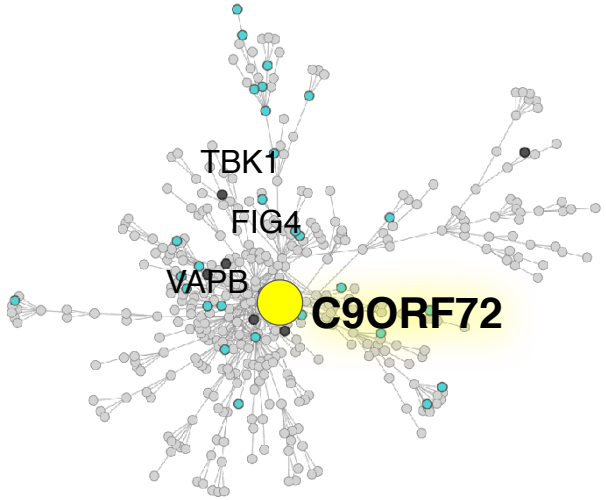
Recent advances in human genetics + biomarkers have fueled new breakthroughs. ALS is at a turning point.

Our platform discovered a new cause of C9orf72 ALS.

We discovered a gene network from ALS patient spinal cords

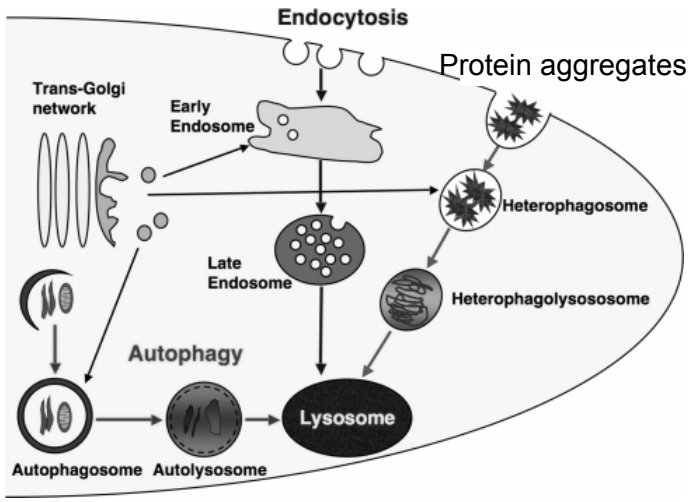


983 post-mortem brains and spinal cords (ALS patients + controls)

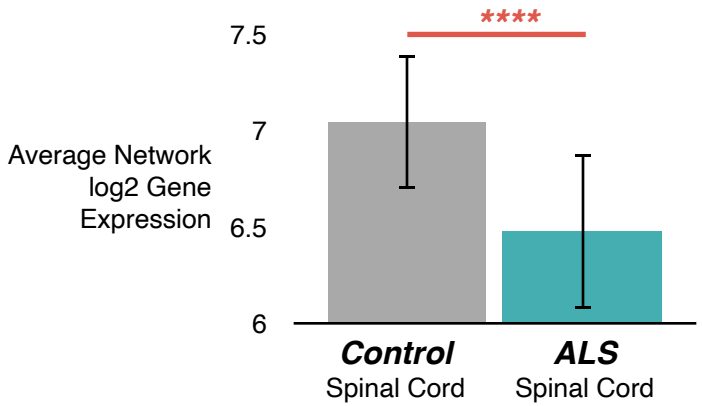


Endolysosomal Genes *(2.3x enrichment)*

This network is enriched for lysosomal genes…

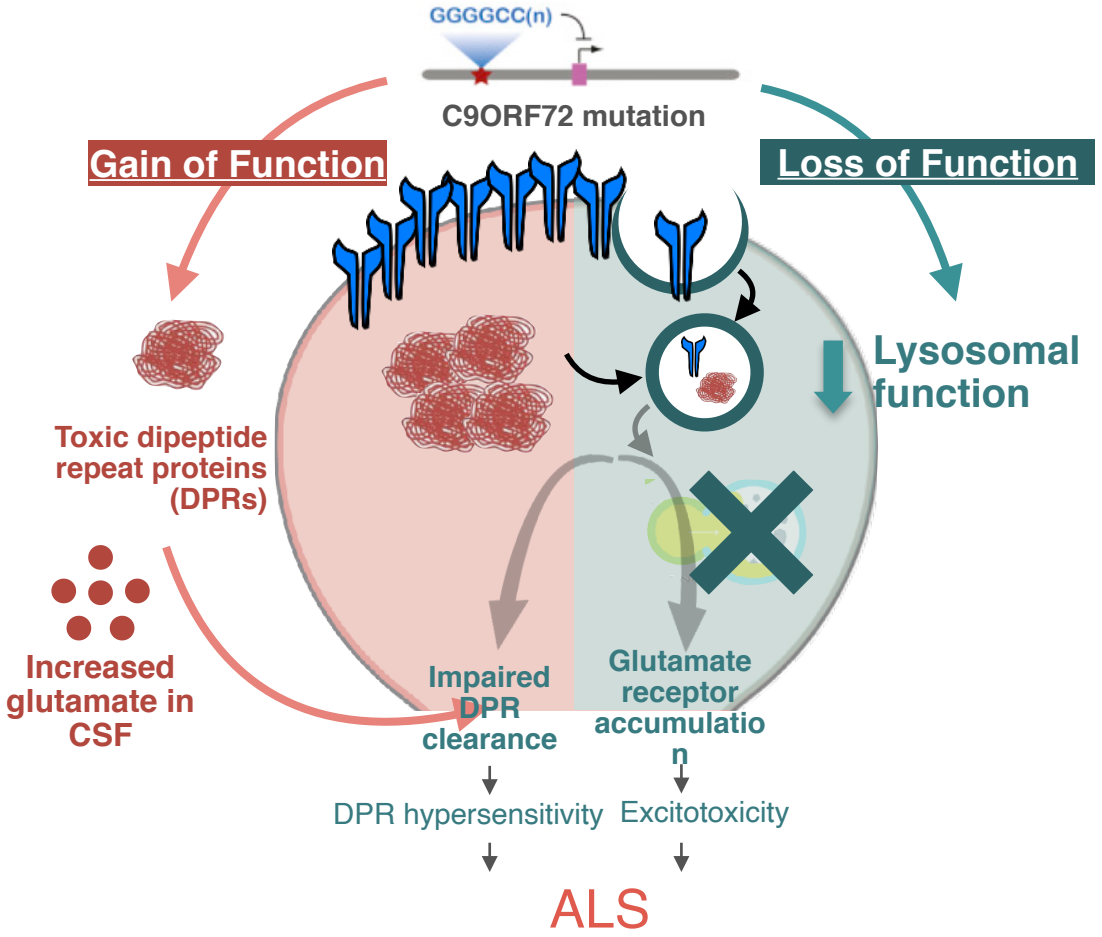


…and highly down regulated in patient spinal cord

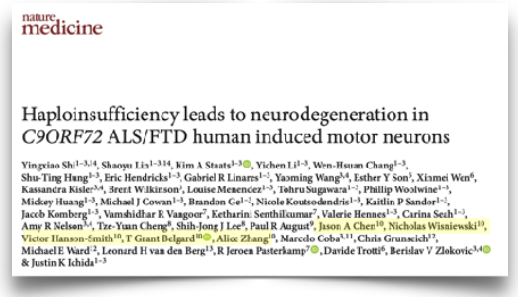


C9orf72 mutations causes ALS via loss of lysosomal function.

In 2018, we revealed a key missing piece of ALS pathogenesis: loss of lysosomal function

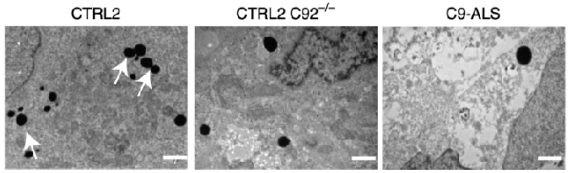


Published in Nature Medicine in 2018 (Shi et al.)


nature medicine

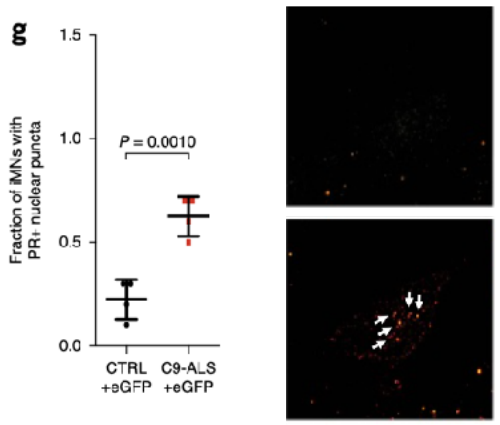
Haploinsufficiency leads to neurodegeneration in *C9ORF72* ALS/FTD human induced motor neurons

Lysosome formation is impaired in C9ORF72 ALS patient neurons…

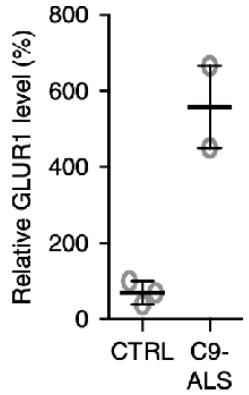


…which results in DPR and glutamate receptor accumulation.

Dipeptide repeat proteins (DPRs)



Glutamate receptors



TARGET ID

Our platform identified PIKfyve as a new target in ALS.

Human Validation

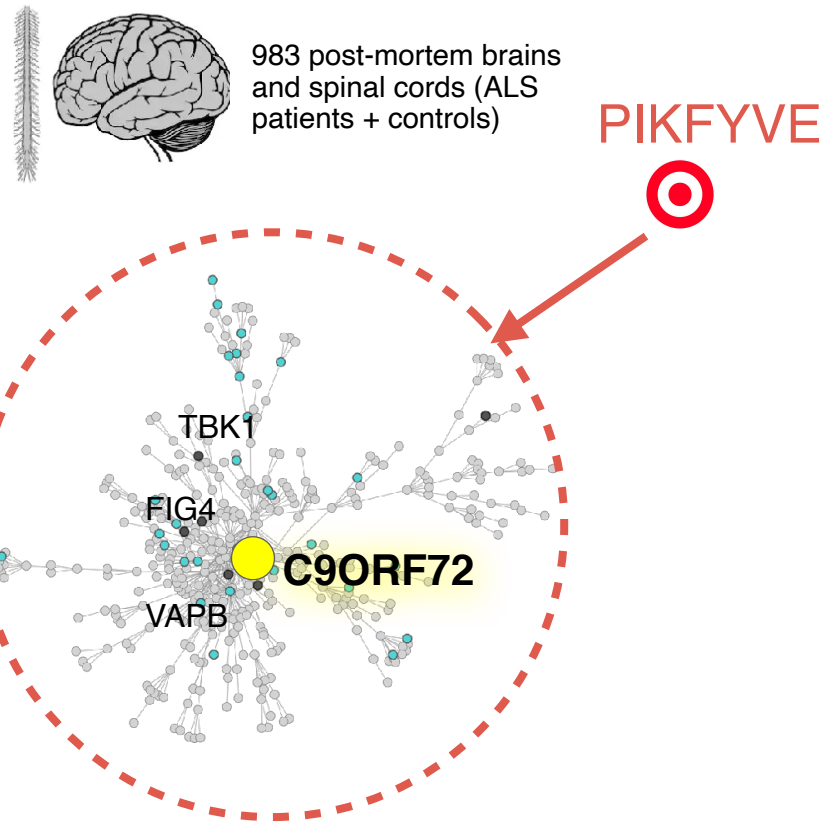
- ✓ **Human tissue:** Found from ALS patient spinal cords
- ✓ **Human genetics:** Mutations in PIKfyve/FIG4 complex cause ALS
- ✓ **Human validation:** PIKfyve inhibition slows ALS patient-derived neuron death

Strong Biological Rationale

- ✓ **Genetic convergence** on lysosomal function in ALS
- ✓ **Preclinical POC**: Endolysosomal deficiency drives ALS
- ✓ **Target validation:** PIKfyve is a known regulator of endolysosomal biology

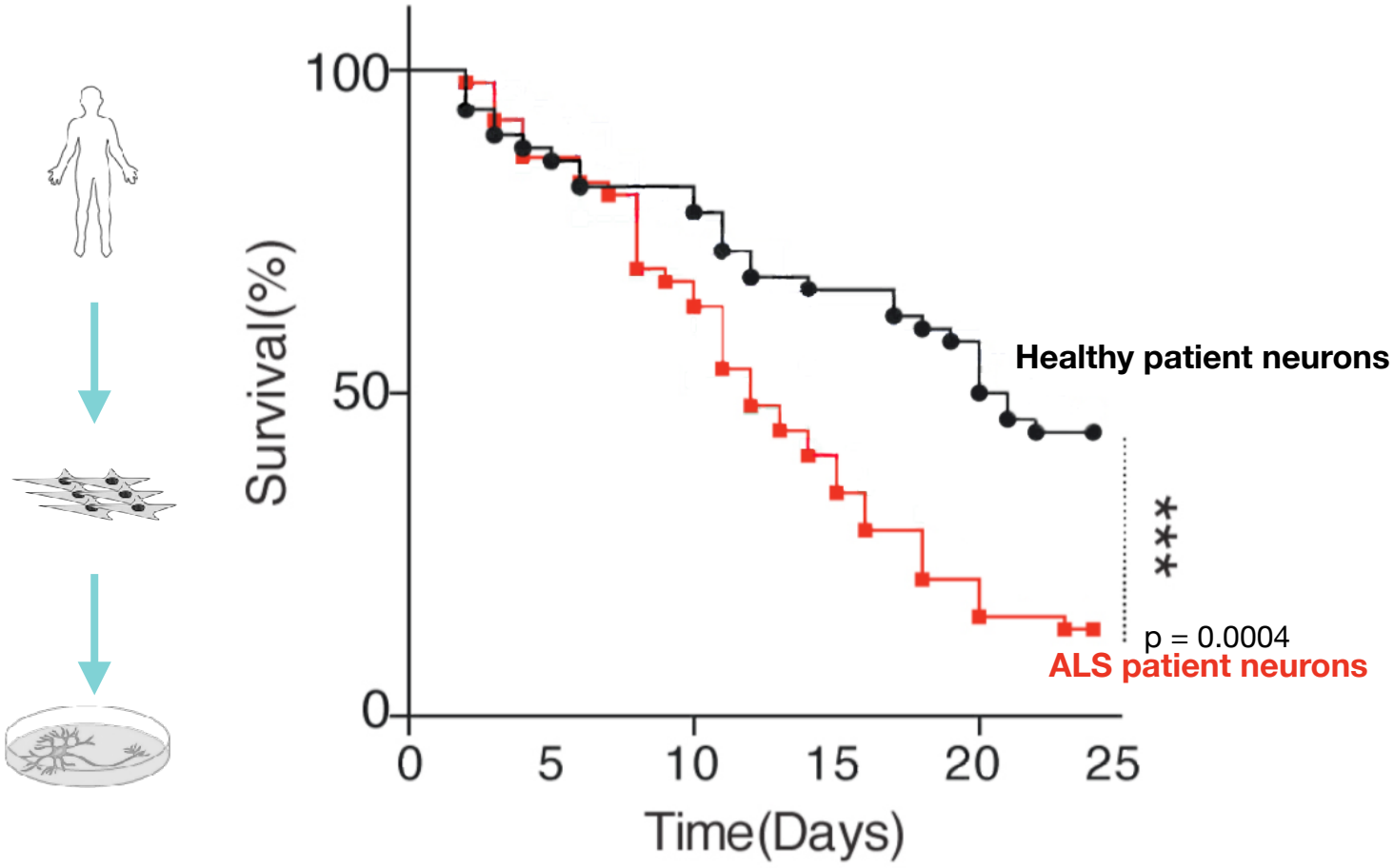
Tractable Development Path

- ✓ **Safety**: PIKfyve inhibitors have been dosed in > 800 patients
- ✓ **Druggable** with available chemical matter
- ✓ **Biomarker** enabled to measure PIKfyve activity

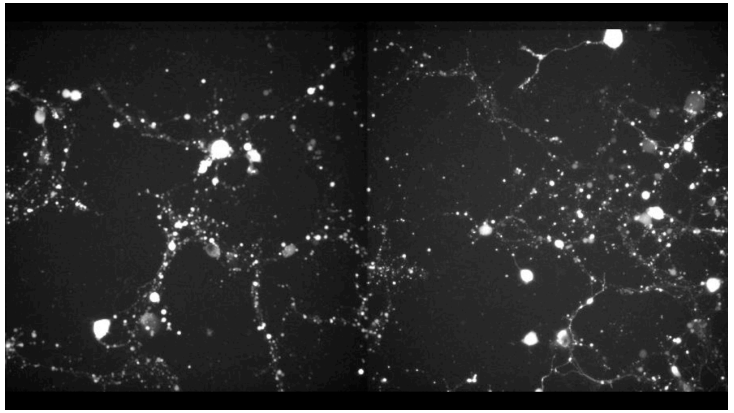


= Greater Probability of Clinical Success

PIKfyve inhibitors fully restore neurodegeneration in ALS patient neurons.

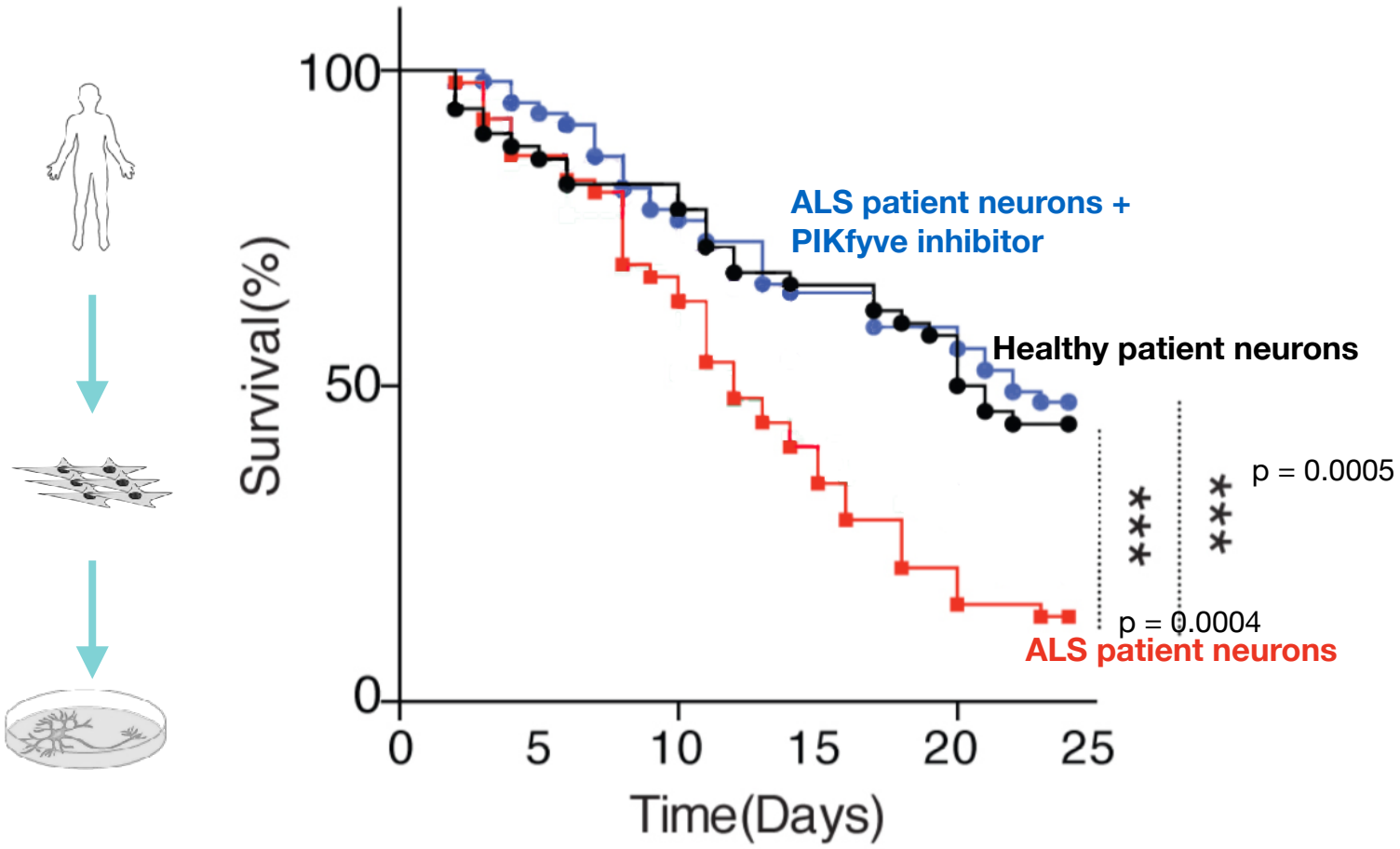


C9orf72 patient neurons

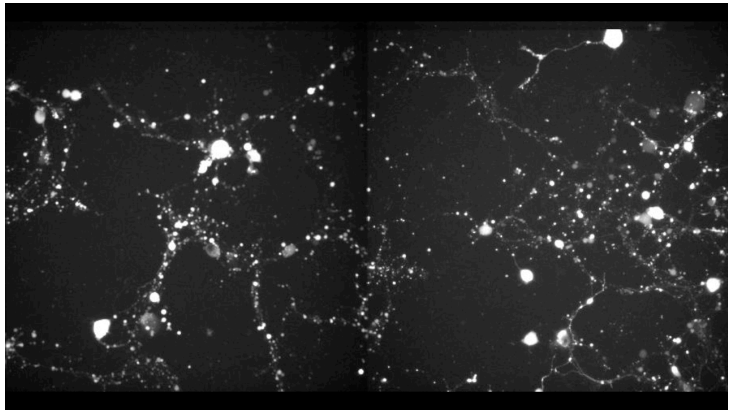


Shi et al. (2018) *Nature Medicine*

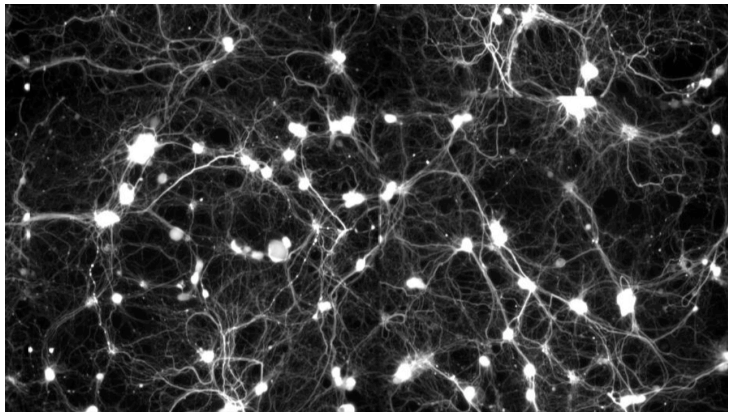
PIKfyve inhibitors fully rescue neurodegeneration in ALS patient neurons.



C9orf72 patient neurons



C9orf72 patient neurons + PIKfyve inhibition



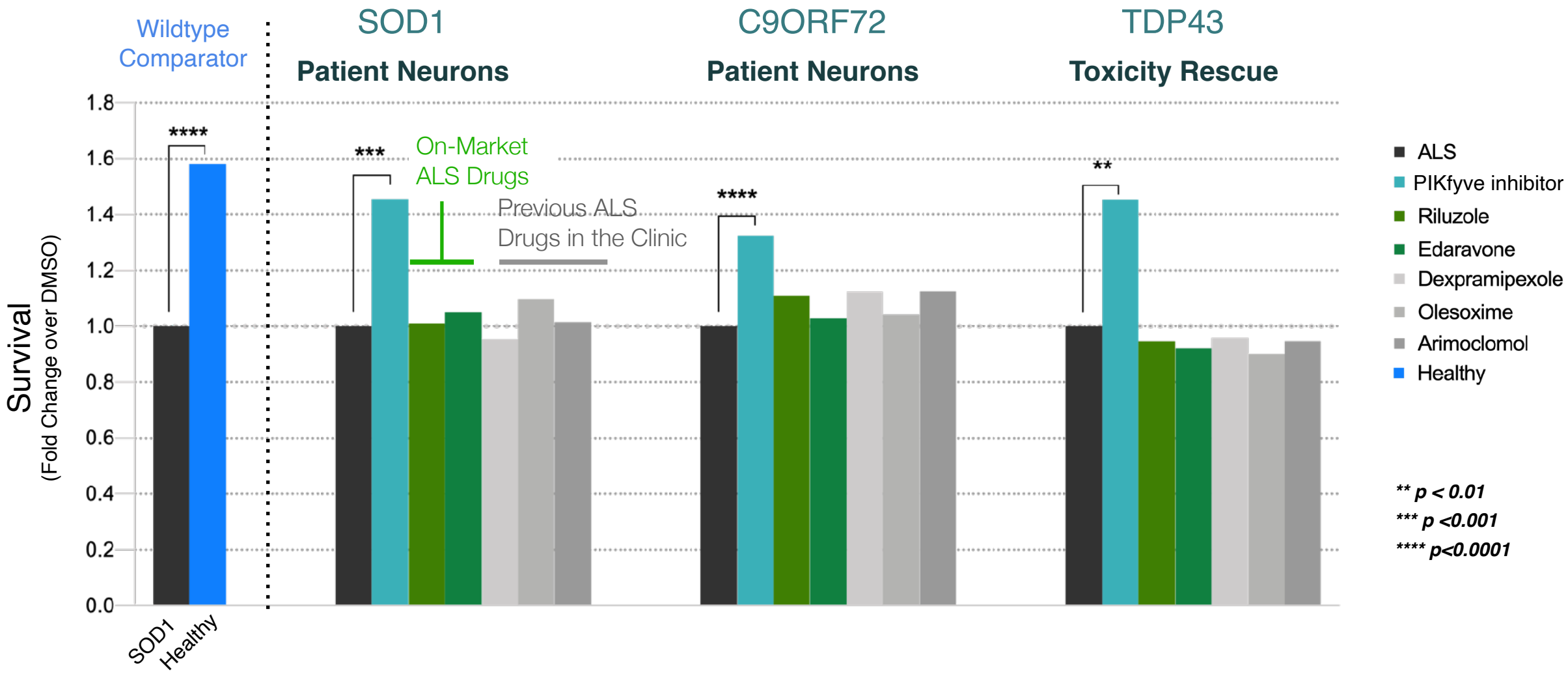
Shi et al. (2018) *Nature Medicine*

COMMERCIAL

Preclinical data supports a therapeutic benefit in broad ALS populations.

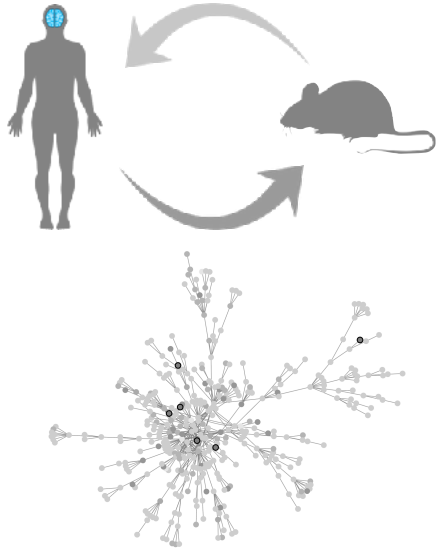
COMMERCIAL

Verge PIKfyve inhibitors outperform on-market ALS drugs.

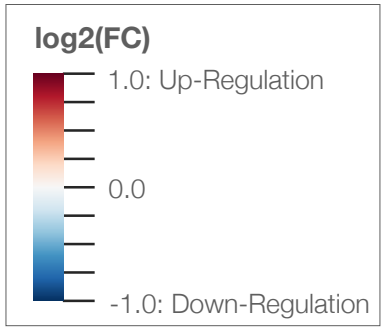


Our drugs reverse the disease signature found in patients.

The C9 disease signature is also down regulated in sporadic patients



PIKfyve inhibition counteracts the C9 disease signature in a mouse model of sporadic pathology



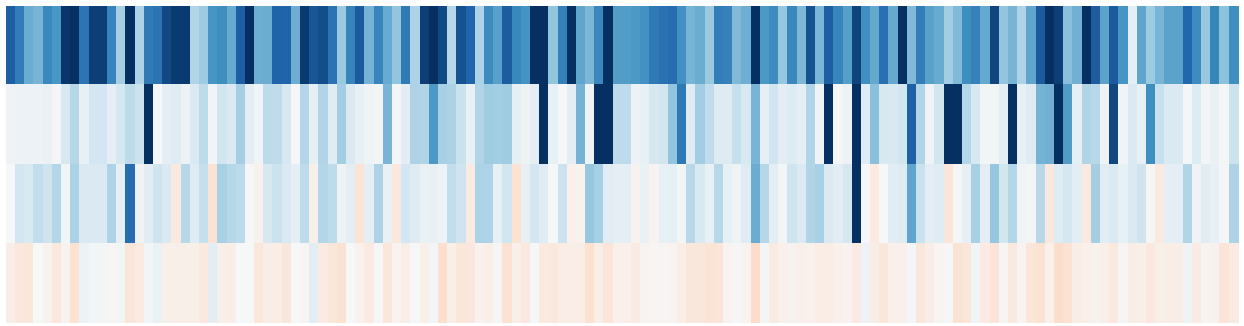
Spinal Cord: ← Genes in **Verge ALS Signature** →

C9orf72 ALS patients

Sporadic ALS patients

TDP43 Mice

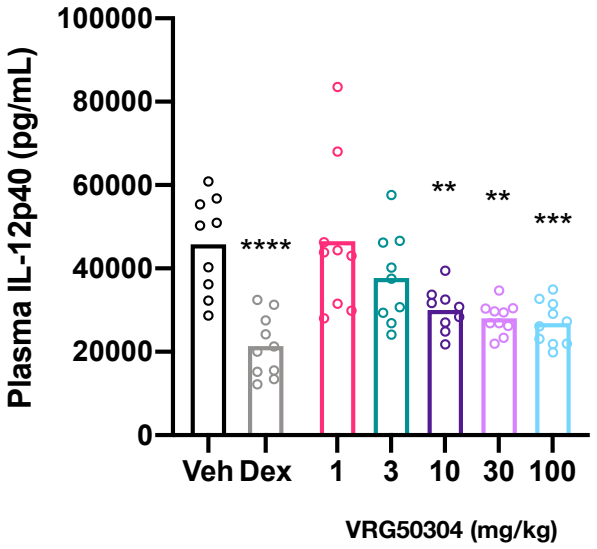
TDP43 Mice + **PIKfyve inhibitor**



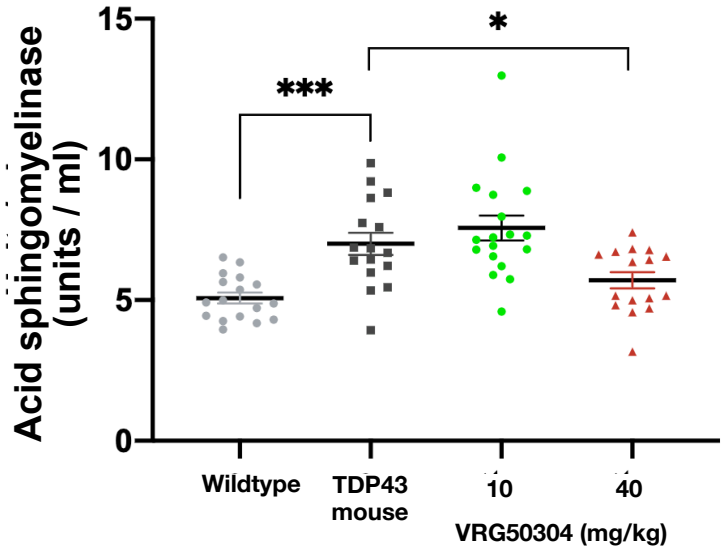
TRANSLATION

Dose-dependent changes in pharmacodynamic biomarkers of treatment response *in vivo*.

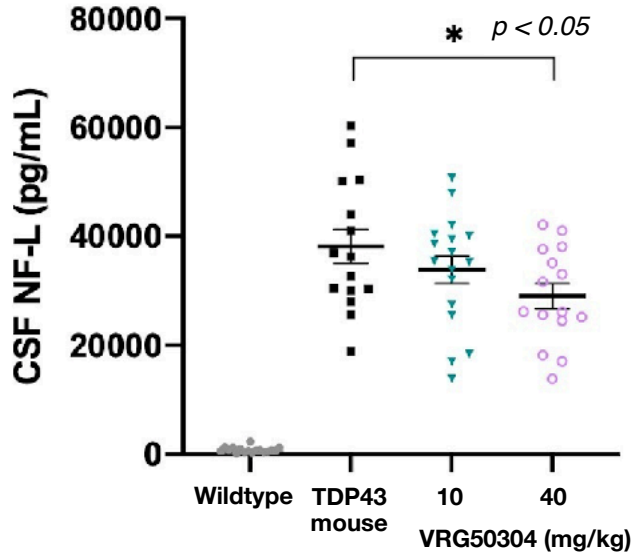
Verge compounds achieve full **target engagement** *in vivo*



Verge compounds restore biomarkers of **lysosomal dysfunction** in an ALS animal model



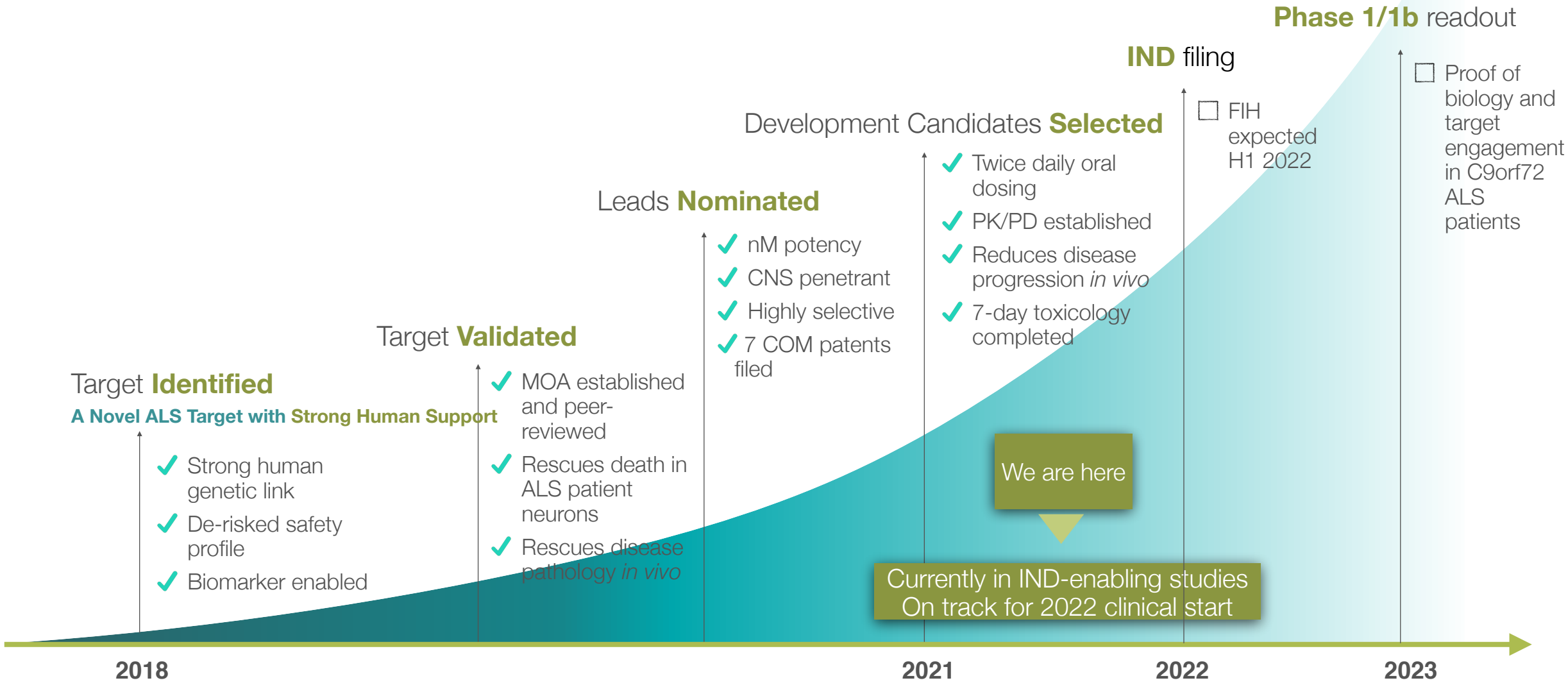
We are the first to reduce markers of **disease progression (NFL)** in the TDP43 mouse.



These markers will be used in our clinical studies to de-risk common causes of clinical failures and provide early indicators of success.

PROGRESS

From platform to development candidate in three years.



VERGE GENOMICS

Better drugs, faster.
For patients who can't wait.