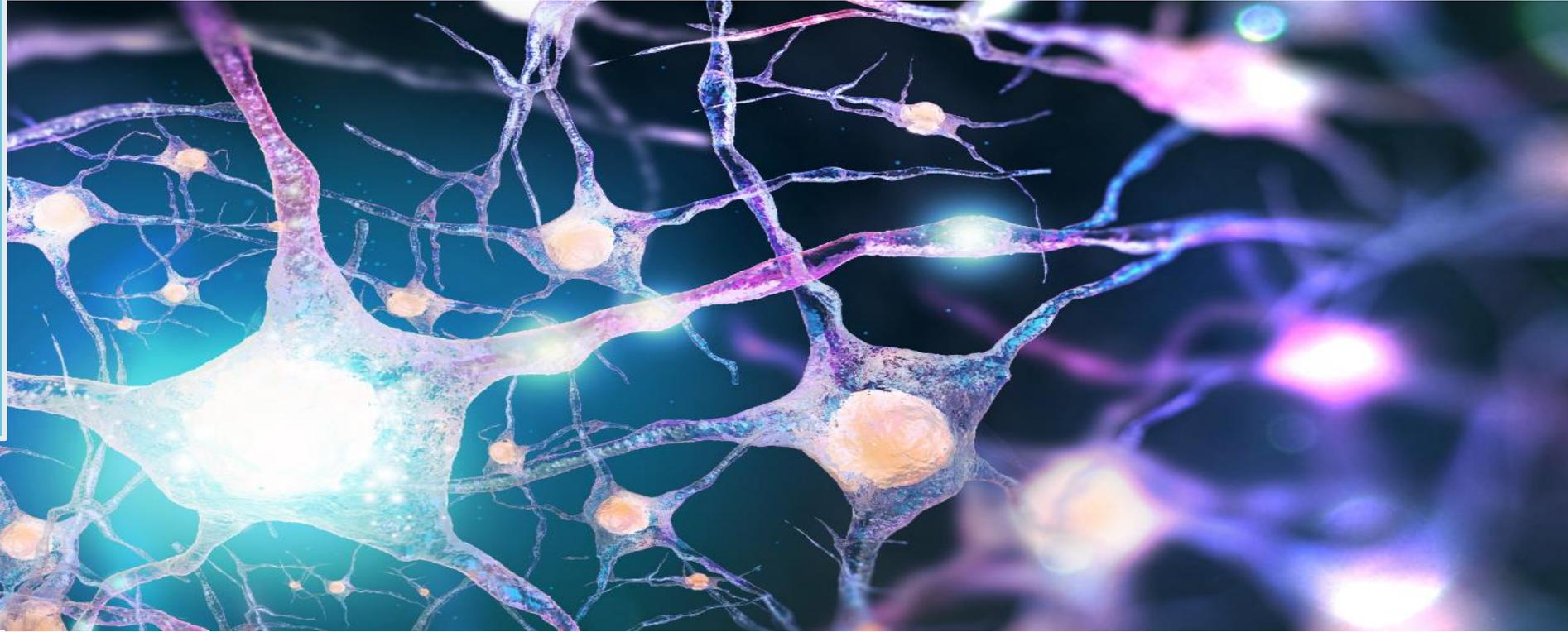


“We are a responsibly-driven company focused on achieving the most efficient development of products that address significant unmet needs in CNS disorders and in rare diseases”



SEELOS **St**  
THERAPEUTICS

# SEELOS THERAPEUTICS

SLS-005 (trehalose injection, 90.5 mg/mL for intravenous infusion) for the Treatment of Familial and Sporadic ALS

# FORWARD-LOOKING STATEMENTS

This presentation includes certain forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995. These forward-looking statements include, but are not limited to, statements regarding the intent, belief or current expectations of Seelos Therapeutics, Inc. ("we," "us," "our," the "Company" or "Seelos") and our management team. These forward-looking statements involve known and unknown risks, uncertainties and other important factors that may cause the actual results, performance or achievements of the Company to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

Words such as “anticipates,” “believes,” “forecasts,” “potential,” “goal,” “contemplates,” “expects,” “intends,” “plans,” “projects,” “hopes,” “seeks,” “estimates,” “strategy,” “continues,” “ongoing,” “opportunity,” “could,” “would,” “should,” “likely,” “will,” “may,” “can,” “designed to,” “future,” “foreseeable future” and similar expressions and variations, and negatives of these words, identify forward-looking statements. These forward-looking statements are based on the expectations, estimates, projections, beliefs and assumptions of our management based on information currently available to us, all of which are subject to change. These forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results to differ materially from the results contemplated by the forward-looking statements. Many of the important factors that will determine these results and values are beyond our ability to control or predict. You are cautioned not to put undue reliance on any forward-looking statements. Except as otherwise required by law, we do not assume any obligation to update any forward-looking statements.

For additional information about factors that could cause actual results to differ materially from those described in the forward-looking statements, please refer to the Company’s filings with the Securities and Exchange Commission, including the risk factors contained in the Company’s most recent Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 and the Company’s Annual Report on Form 10-K for the year ended December 31, 2020.

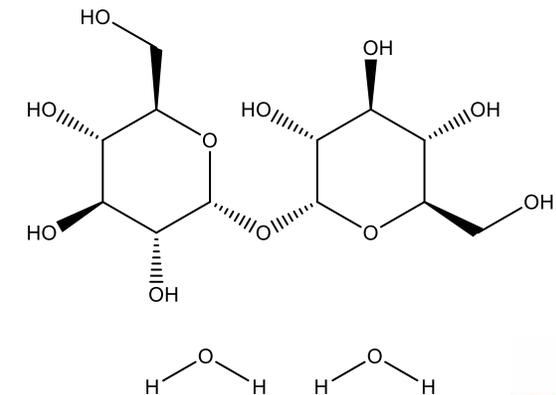
This presentation is not an offer to sell or the solicitation of an offer to buy, any securities.

# Intravenous Trehalose Disclosure

- IV trehalose is an investigational drug being used in this study
- IV trehalose is not approved for treatment of any disease in any country and no regulatory agencies have determined that it is safe and effective
- Taking trehalose by mouth is not equivalent to receiving an infusion of IV trehalose
- There may be side effects or other safety concerns with IV trehalose that are unknown, unexpected or unanticipated

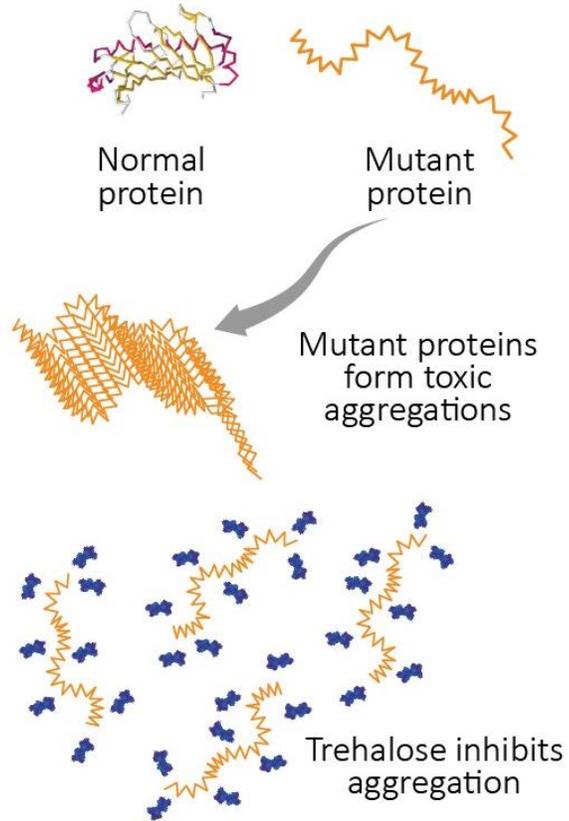
# What is TREHALOSE ?

- Trehalose is a disaccharide composed of 2 glucose molecules linked together
- Found extensively in nature
- Humans do not make trehalose, but can metabolize it
- Oral trehalose is not absorbed due to breakdown by gut trehalase's (<0.5%)
- Trehalase's are found in the gut, kidney and liver and breakdown trehalose to the 2 glucose molecules
- In this study trehalose is administered IV to bypass the gut trehalase enzymes
- Trehalose penetrates muscle and brain

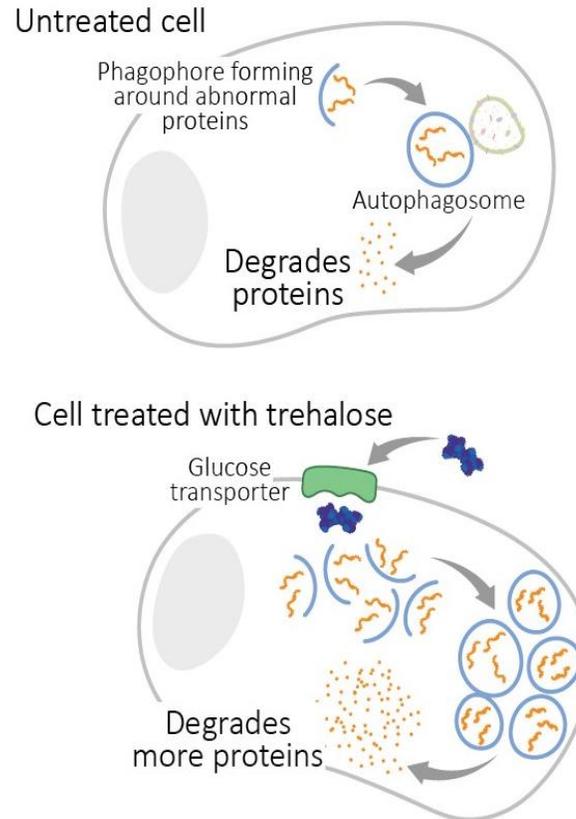


# TREHALOSE MECHANISM OF ACTION

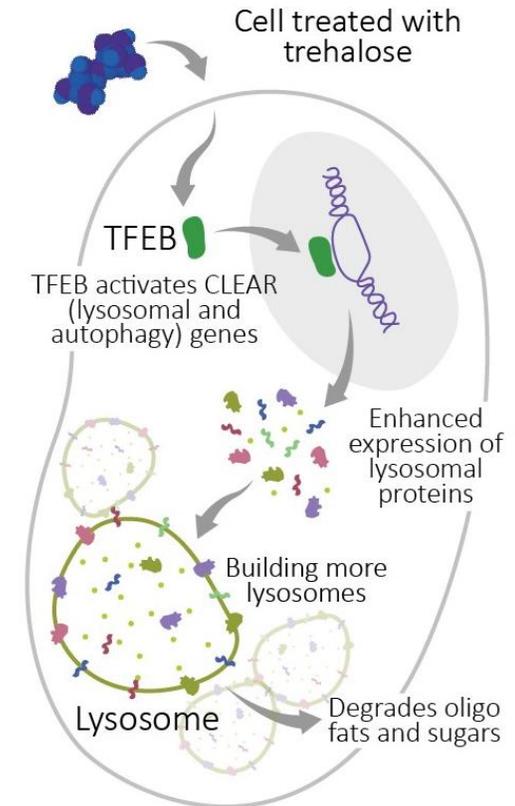
## Protein stabilization



## Immediate enhancement of autophagy



## Prolonged enhancement of lysosomal pathways thus autophagy



# What is Autophagy

- From the Greek autóphagos meaning "self-devouring"
- Autophagy is the breakdown of cellular elements to be used to prevent starvation
  - When a cell needs energy and none is available, starvation scenario, the cell will breakdown cellular components to create the needed energy
- Thus, autophagy is a survival mechanism

# Why is Autophagy important in ALS

- *Autophagy* is also the natural process that removes unnecessary and abnormal proteins in cells
- Autophagy is impaired in ALS and leads to protein aggregates in cells such as SOD1 and TDP-43 that impair cellular function
- Several animal studies have shown that treatment with trehalose can activate *autophagy* and clear toxic protein aggregates

# Trehalose treatment in animal models of ALS

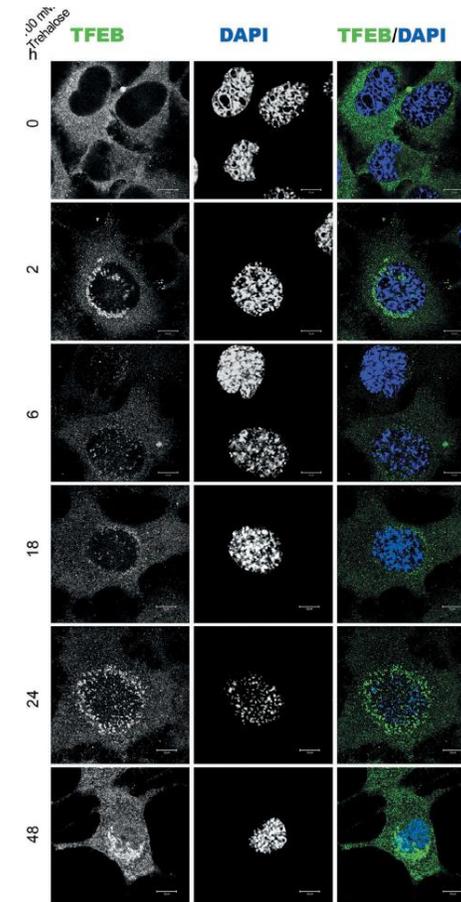
- Treatment with trehalose in the mouse\* model of ALS and cell lines has demonstrated:
  - Activation of autophagy pathways
  - Delayed onset of disease
  - Prolonged survival
  - Reduced aggregation of SOD1 protein
  - Reduced motor neuron loss
  - Improved motor function
  - Preserved weight

\*Mice can be treated with oral trehalose since they do not have enzymes that breaks down trehalose in the gut

# *“Trehalose induces autophagy via lysosomal-mediated TFEB activation in models of motoneuron degeneration”*

## Immortalized motor neuron cell line (NSC34)

- Trehalose exposure
  - TFEB translocated to nucleus
  - Activates genes for autophagy
  - Increased clearance of TDP-43



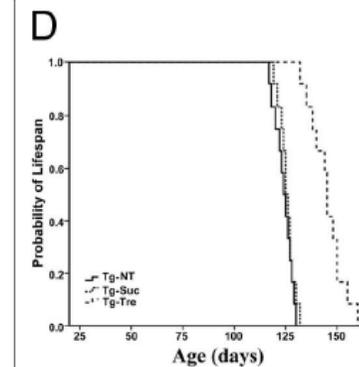
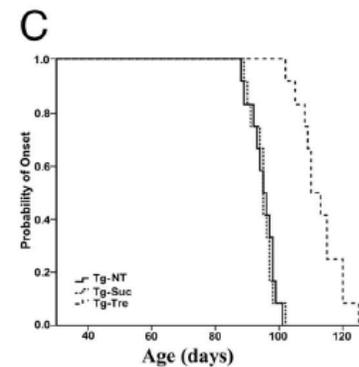
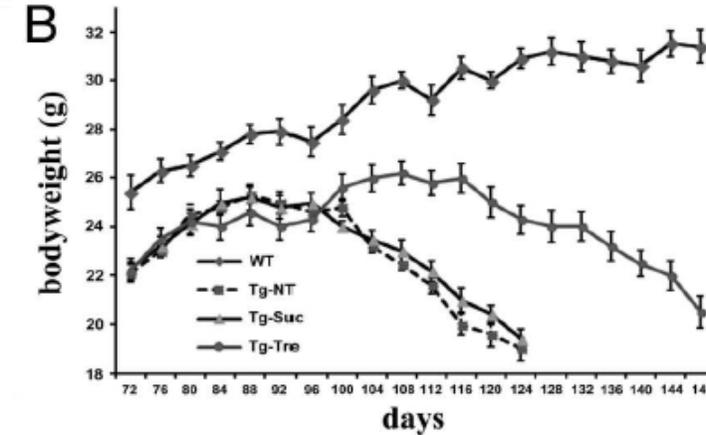
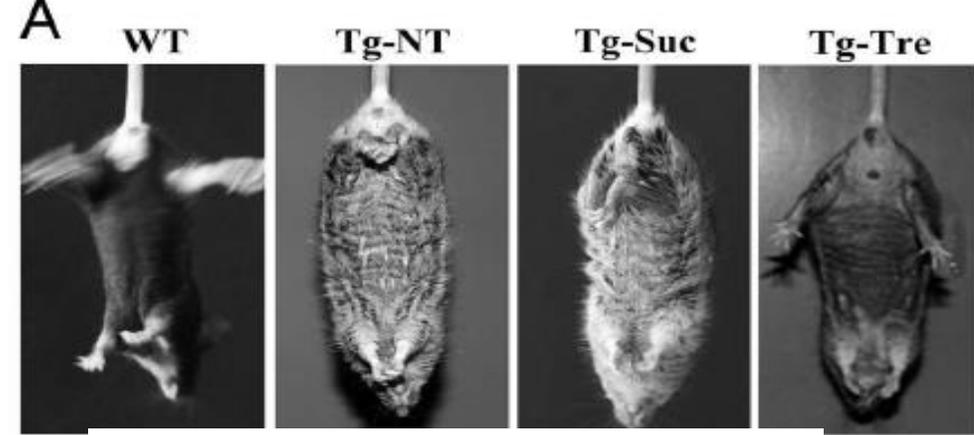
Late effect of trehalose treatment

Rusmini 2019 Autophagy Vol 14 No 4 631-651 2019; Wang 2018 Neurotoxicity Res 34:109-120

# TREHALOSE IN ALS

MTOR-independent, autophagic enhancer trehalose prolongs motor neuron survival and ameliorates the autophagic flux defect in a mouse model of ALS

- Treatment of mice with oral trehalose\*
  - Delayed onset of disease C
  - Prolonged survival D – E
  - Preserved muscle strength A
  - Preserved weight B
  - Reduced motor neuron loss and skeletal denervation
  - Improved autophagy flux
  - Reduced aggregation of SOD1 and SQSM1/p62



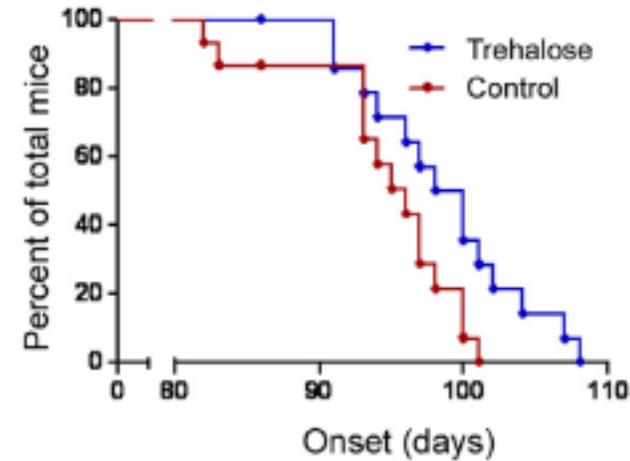
	Tg-NT	Tg-Suc	Tg-Tre
Disease onset	95.00 ± 1.15	94.92 ± 1.05	112.70 ± 1.93 <sup>**, &amp;&amp;</sup>
Lifespan	124.10 ± 1.22	125.60 ± 1.05	145.20 ± 2.34 <sup>**, &amp;&amp;</sup>
Disease Duration	29.82 ± 1.84	30.68 ± 1.50	32.88 ± 2.24

\*Mice can be treated orally since they do not have gut trehalase

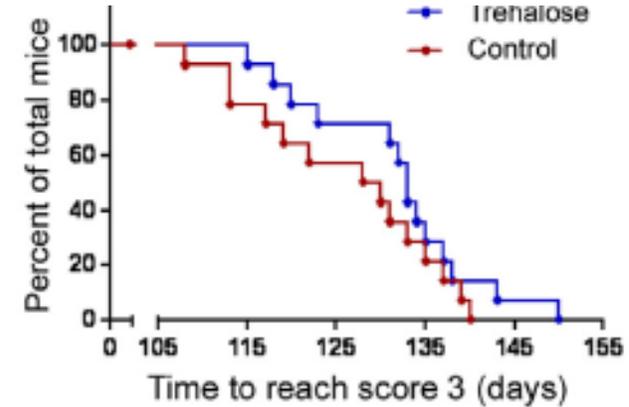
# TREHALOSE IN ALS

Trehalose decreased mutant SOD1 expression and alleviated motor deficiency in early but not end-stage ALS in a SOD1-G93A mouse model

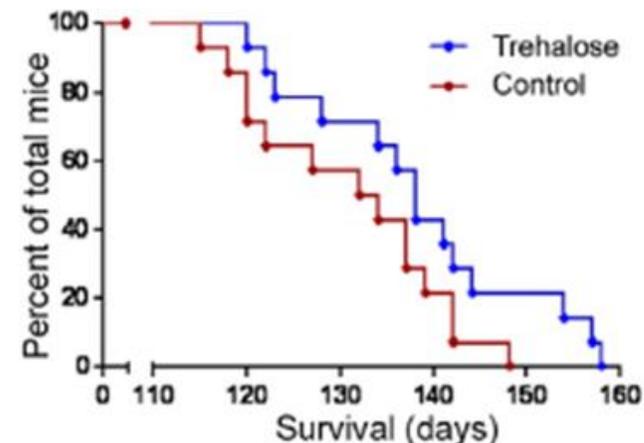
- Decreased expression on SOD1 and p62 in spinal cord
- Increased LC3-II (Microtubule-associated protein 1A/1B-light chain 3)
  - Involved in autophagy
- Postponed disease onset A
- Delayed progression of disease B
- Prolonged survival C
- Inhibited microgliosis and astrogliosis
- Preserved motor function



A



B



C

# IV Trehalose Summary

- Trehalose is a naturally occurring sugar composed of 2 glucose molecules
- IV trehalose is an investigational drug being used in this study
- Lab data suggest that IV trehalose has potential for the treatment of ALS
- We are participating in HEALEY ALS Platform Trial to find out if IV trehalose is safe and effective in people living with ALS

Questions