



**Testing the
Neuroprotective
Effect of a Lead
Compound Using *C.
elegans* for Fast and
Cost-Effective
Answers**

Customer Story



InVivo Biosystems

Overview

Dr. Marius Galyan is the founder and CEO of Galyan Bio, Inc., a research company on a mission to discover new therapies for neurodegenerative diseases, such as Alzheimer's and Huntington's Disease. Dr. Galyan and his team had discovered a compound originally developed for Huntington's that removes pathologic proteins in addition to activating novel neurons, giving it a neuroprotective effect.

One of the major contributing factors to how humans age is that, as we age, our ability to efficiently degrade pathological proteins decreases. Since the compound that Dr. Galyan had found seemed to remove the pathological proteins, he believed that the neuroprotective effect of this compound had intriguing implications on longevity, and required further study.

Challenge

Dr. Galyan wanted to test this hypothesis, but he recognized that generating a realistic longevity model is very difficult, and that traditional models such as mice are both expensive and time intensive. After doing his research into alternate animal models, he landed on *C. elegans* as a cost-effective and fast way to test his compound. While *C. elegans* seemed like the perfect model to test his hypothesis, for someone who has never used the model before it can be very challenging to run lifespan assays.

Solution

Dr. Marius Galyan chose to leverage the InVivo Biosystems Longevity Platform to assess a single select compound for possible effects upon *C. elegans*' longevity and healthspan.

Benefits

Thanks to InVivo Biosystems, Dr. Galyan now has the data necessary to present to investors to fund additional research into the compound. Additionally, he was able to use the data to submit a patent application on the compound in September of 2021.

Having a family history of Alzheimer's, Dr. Galyan was motivated to pursue an MD in neurology and has focused his career on researching neurodegenerative diseases. He began by investigating Huntington's Disease, since the models for that disease are more established, however, in the future he hopes to expand his research into other diseases such as Parkinson's and, of course, Alzheimer's Disease.

While he may be a trained MD, Dr. Galyan also has a taste for entrepreneurship and founded Avergen Pharmaceuticals in 2015. In 2019 he founded his current company, Galyan Bio Inc., a company focused on researching small molecules affecting neurodegenerative diseases.

Dr. Galyan's current research began in 2015, when he set out to find small molecules that could act as a therapeutic for Huntington's Disease by attaching to a mutant protein that is a marker of the disease. In order to narrow down which compounds to screen, Dr. Galyan sought out a friend of his, Dr Jordi Mestres, who has an *in silico* compound screening system. The mutant Huntingtin protein was placed on a chip (Biacore) and the compound binding was measured via a signal. The stronger the signal, the stronger the binding, and the more likely that that would be a successful compound. Typically, with library screens you are screening hundreds of thousands of compounds, but Dr. Galyan only screened 49 compounds. Despite this, the compound screen returned hits in nine of the 49 compounds, six of which were dose dependent, meaning there was a visible change in response that correlated to a change in dosage. From there, they did further research into these six compounds to try and hone in on which of those six would be the best candidate. During this research, Dr. Galyan's team found that one of the six compounds also activated novel neurons, giving the compound a neuroprotective effect. This was intriguing to Dr. Galyan, as he thought this could indicate another use for the compound - producing a positive effect on longevity (as our inability to degrade those pathological proteins is one of the major aging pathways).

Dr. Galyan and his team wanted to conduct a pilot study to see if their hypothesis about the compound's positive effect on longevity was true, but longevity studies are difficult. Just beginning can be daunting: it is difficult to get a realistic model, and the studies themselves can be challenging to set up and require a lot of time and money. Traditionally, mice models are used in longevity studies, but "aging studies in mice are expensive and take a lot of time, so I wanted to see if there's an effect in *C. elegans* because you get faster results and it's cheaper".

“ Before investing that amount of money and time, we wanted to see if there is a legitimate case for this ”

While there are numerous alternative models for studying longevity, *C. elegans* are an ideal model for longevity studies as they have a short lifespan, morphological simplicity, and are very easy to maintain and genetically modify. Dr. Galyan decided the *C. elegans* model would be the most effective model for his purposes as *C. elegans* are a well-established model, so there were already a number of studies using them as a stepping-stone in aging research before moving into mammalian models.

“*[Modeling first] in C. elegans would be, of course, faster than doing it immediately in mice. So, it's my hope that we can get faster results and good meaningful results on which we can base further research*”

Utilizing a model whose data could be easily compared was an important factor to Dr. Galyan as it was in line with published literature, since “a lot of compounds [have been] tested in *C. elegans* and then in mammals”. This meant there was already a number of studies and available data out there for Dr. Galyan to reference as he proceeded with his investigation.

While he has worked with a number of animal models before, Dr. Galyan had never worked with *C. elegans*. Somewhat familiar with the model, he decided to do a small study himself to see what it was like working with the model, and realized pretty quickly that it would be much easier to outsource these needs to a company who not only had *C. elegans* experience, but the infrastructure in place to support a longevity assay.

“*I thought it would be best to find a company which already has a running system [for testing C. elegans], so I looked around and came up with your company!*”

Having decided to take a multi-model approach to this study, Dr. Galyan was pleased with the results produced by working with *C. elegans* for the pilot phase. Dr. Galyan was able to act quickly, making further improvements and refinements to the compound before moving into rodent models. “We can get from the *C. elegans* model a direction for how to better draft a study in rodents to get a better understanding and to doctor in a way which then gives you the right data, which you can then use to finalize the drug status as a drug candidate. And that helps to try to design the study for rodents”.

“ *The C. elegans model was very important to see that...the median lifespan improved significantly. That's the central outcome which vindicates and justifies a bigger study in rodents* ”

The Data

The data collected on Dr. Galyan's compound gives a hint at how effective the compound is and whether or not he should pursue additional studies. We at InVivo Biosystems, found Dr. Galyan's compound extends the median lifespan and the activity of the worms without extending the maximum lifespan, thus shortening the period of late-life frailty. This indicates that Dr. Galyan's compound is a promising therapeutic candidate.

InVivo Biosystems used a 3-step approach to testing Dr. Galyan's compound. In the first step, we tested for dosage and toxicity. In the second step, we performed a lifespan assay and conducted survival and healthspan analysis using the dosage identified in the first step. The movement assay was one that Dr. Galyan was especially excited about, as it “gives us [the data] for promoting our drug discovery program because we are not only extending the life of the animal, but we are also improving the animal's motility and that's really important”.

The third, and final, step in the data collection included a gene expression analysis. According to Dr. Galyan, “the gene expression data is really important for us, and this will give us information for which direction to further look, because we know the mechanism.... which [will] direct us into what kind of studies and experiments we have to do and how to draft a rodent model study”.

We examined the transcriptional response of Dr. Galyan's compound at multiple levels: individual genes, gene ontologies, and cellular pathways. Analysis of data identified two closely linked longevity associated pathways, and the effect of Dr. Galyan's compound on *C. elegans* lifespan is supported by the gene expression data consistent with known longevity pathways.

Dr. Galyan was very pleased with the data provided by InVivo Biosystems, and now has the proof-of-hypothesis he needs to present to investors and pursue additional studies. In fact, Dr. Galyan was able to use the data provided to apply for a patent on the compound in September of 2021.

“ *This gives us a hint of how effective the compound is...and very impressive results were gained* ”

Where will your research go next?

Taking the data provided by InVivo Biosystems into account, Dr. Galyan and his team will further optimize the compound, using in vitro assays in addition to self-reliance with cells, they will come up with new compounds for testing in *C. elegans*, and then finally move into mammalian studies.

“ *Based on [this] information [we will] do further experiments and studies, to further build and strengthen the case, to use our compounds for an anti-aging or longevity drug* ”

During the project, our team provided regular updates to Dr. Galyan about the project and held meetings to explain the data as well. Since Dr. Galyan was unfamiliar with the *C. elegans* model, having someone explain the data and be there to answer any questions he had was really important for him. Dr. Galyan believes that working with InVivo Biosystems and using the *C. elegans* model “gave us the information [we needed] to better improve our and optimize our compounds to the final clinical candidate stage”.

At the end of the day, Dr. Galyan hopes this compound will have meaningful results with patients, because “I’m...trained as a medical doctor. So, my main concern is to get something which works properly, and which has a big effect for patients. And that’s, of course, what I want to do. It’s not just for the art of science, but we want to have something tangible at the moment”.

With the data generated by InVivo Biosystems, “it can be said that this compound has the potential for healthy aging and I think that’s very important for not only getting older, but being healthy”.

About InVivo Biosystems

An expert in CRISPR genome editing, InVivo Biosystems creates custom genome-edited *C. elegans* and zebrafish models to enable aging, developmental and other disease studies. Our unique living platforms and technologies bridge the gap between cells and mice, providing faster, cost-effective investigations that focus on proof-of-principle experiments for rapid go/no-go decision making, and advance the discovery and early-stage development of new compounds.

What we do

- Deliver scientific data on test results in less than 5 months.
- Produce the best outcome measures for anti-aging products.
- Provide information about mechanisms of action (MoA).
- Support your Marketing and IP claims with real science.

Contact us to start a conversation about how our services can support you.



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