

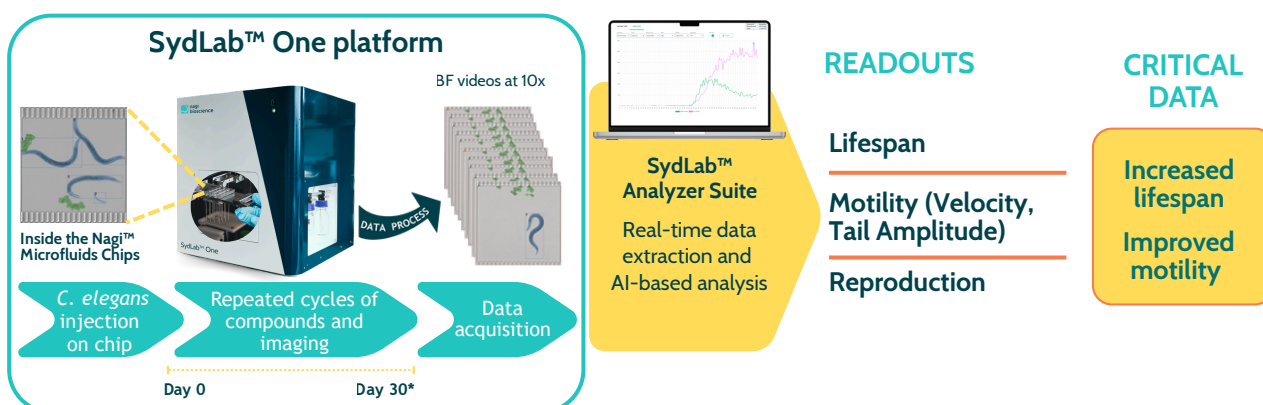
# Exploring combination therapies for longevity: Insights from *C. elegans* screening with SydLab™ One

How Nagi Bioscience delivered key *in vivo* findings for ElixIRA Pharma

ElixIRA Pharma partnered with Nagi Bioscience to evaluate the longevity potential of their lead candidates, E1 and E2, both individually and in combination, across a range of doses. Using our proprietary **SydLab™ One platform**, we conducted a **conclusive study that generated critical insights** into the synergistic effects of these compounds on lifespan and motility in *C. elegans*.

## The Solution: SydLab™ One platform

**SydLab™ One platform** enabled precise, automated, and real-time monitoring of **lifespan and phenotypic biomarkers (motility and reproduction)** using *C. elegans*, a proven model organism for aging studies.

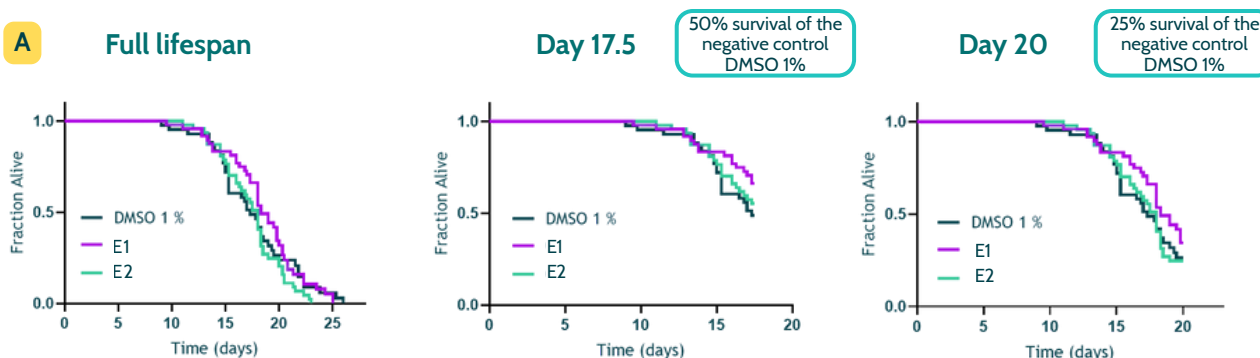


## Results

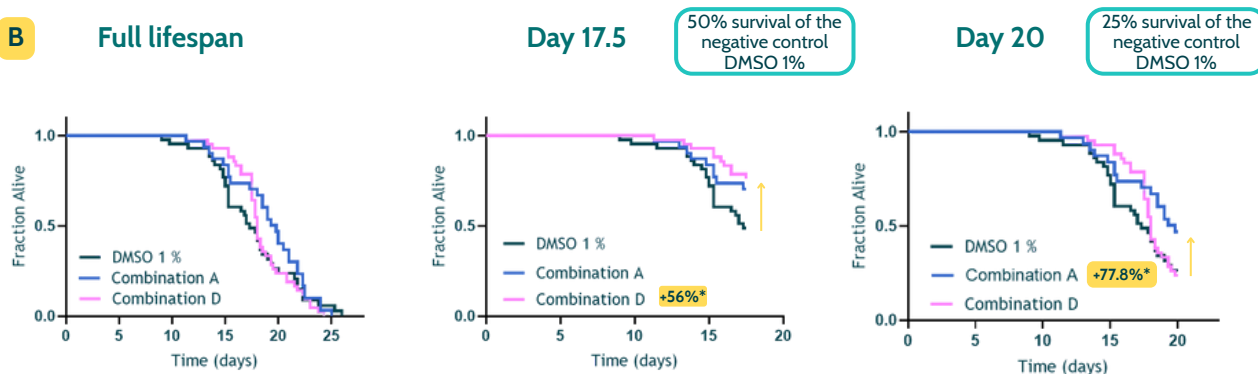
E1 and E2 were tested at specific concentrations along with various dose combinations, allowing the study to examine dose-dependent responses in treated nematodes (not all combinations are shown). The study demonstrated that the combination of E1 and E2 at high doses (combination A) and half of the maximum doses (combination D) resulted in significant synergistic effects on both increasing lifespan and improving motility in *C. elegans*.

### Lifespan monitoring

#### Survival curves



## B Full lifespan

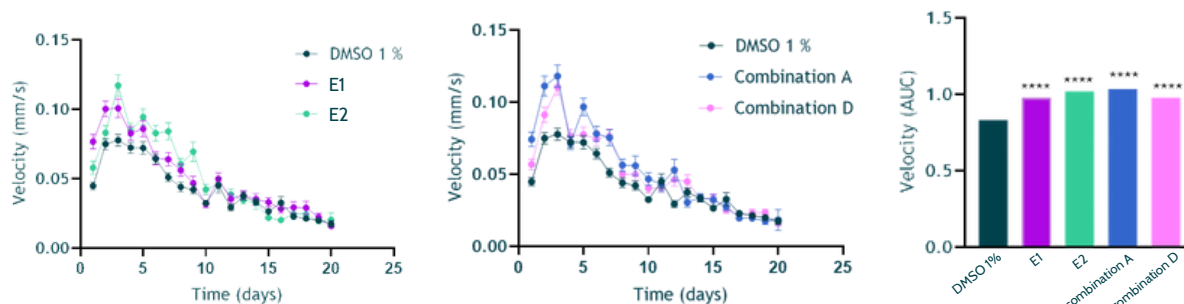


**Figure 1. Effect of E1 and E2 individually (A) or in combination (B) on *C. elegans* lifespan.** Survival curves of nematodes throughout their whole lifespan (left), at day 17.5, which corresponds to 50% survival of the DMSO 1% (negative control) (middle), and at day 20, which corresponds to 25% survival of the DMSO 1% (right). Survival analyses were performed using the Kaplan-Meier method, and the significance of differences between survival curves was calculated using the log-rank test. \* Values show the difference with the DMSO 1% in percentage  $p < 0.05$

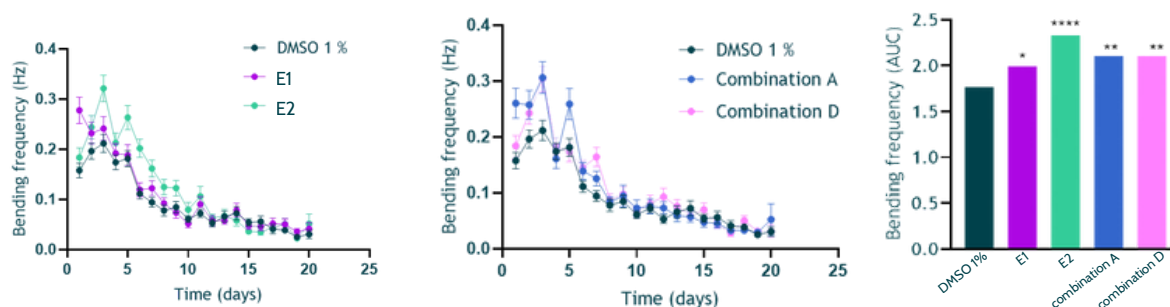
Both tested compounds, whether administered individually or in combination, showed a lifespan-prolonging trend compared to the DMSO 1% (negative control). Notably, when focusing on day 17.5 and day 20, corresponding to 50% and 25% survival of the control population, significant improvements were observed. Specifically, combination D extended median survival (50%), while combination A showed a significant effect at the 25% population survival. These findings suggest that these combination treatments effectively delayed mortality up to these critical stages of the lifespan.

## Mobility

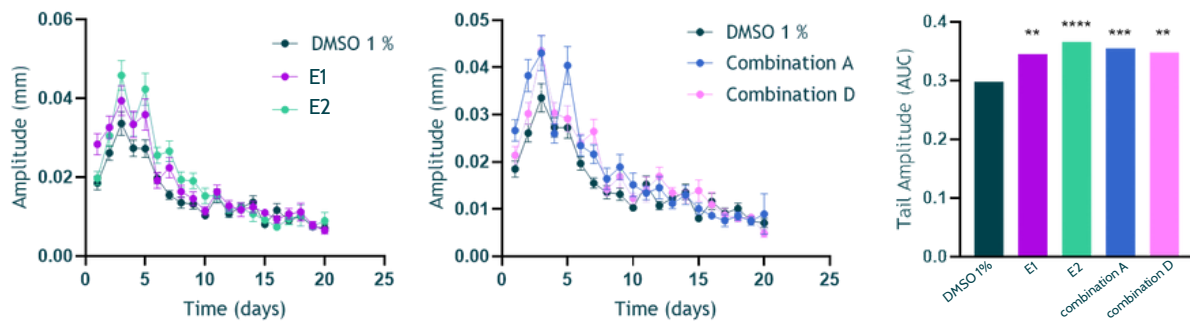
### Velocity



### Bending frequency



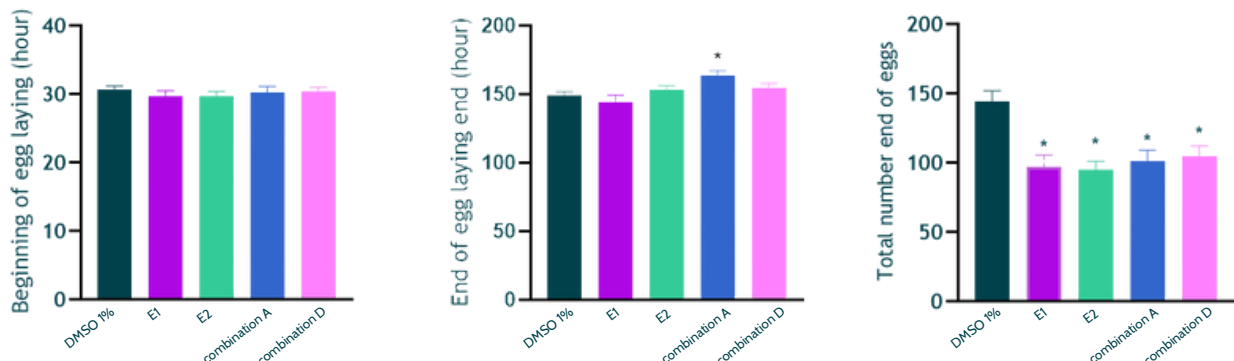
## Tail Amplitude



**Figure 2. Graphical representation of *C. elegans* motility parameters across the lifespan:** Velocity (mm/s), bending frequency, and tail amplitude (mm) were measured longitudinally. Statistical analysis was performed using two-way ANOVA to assess overall differences across curves, followed by Bonferroni's multiple comparisons test. \* p<0.05, \*\* p<0.01; \*\*\* p<0.001; \*\*\*\* p<0.0001.

The overall motility of *C.elegans* populations treated with E1, E2, and both combinations was significantly increased when compared to the negative control (DMSO 1%).

## Reproduction

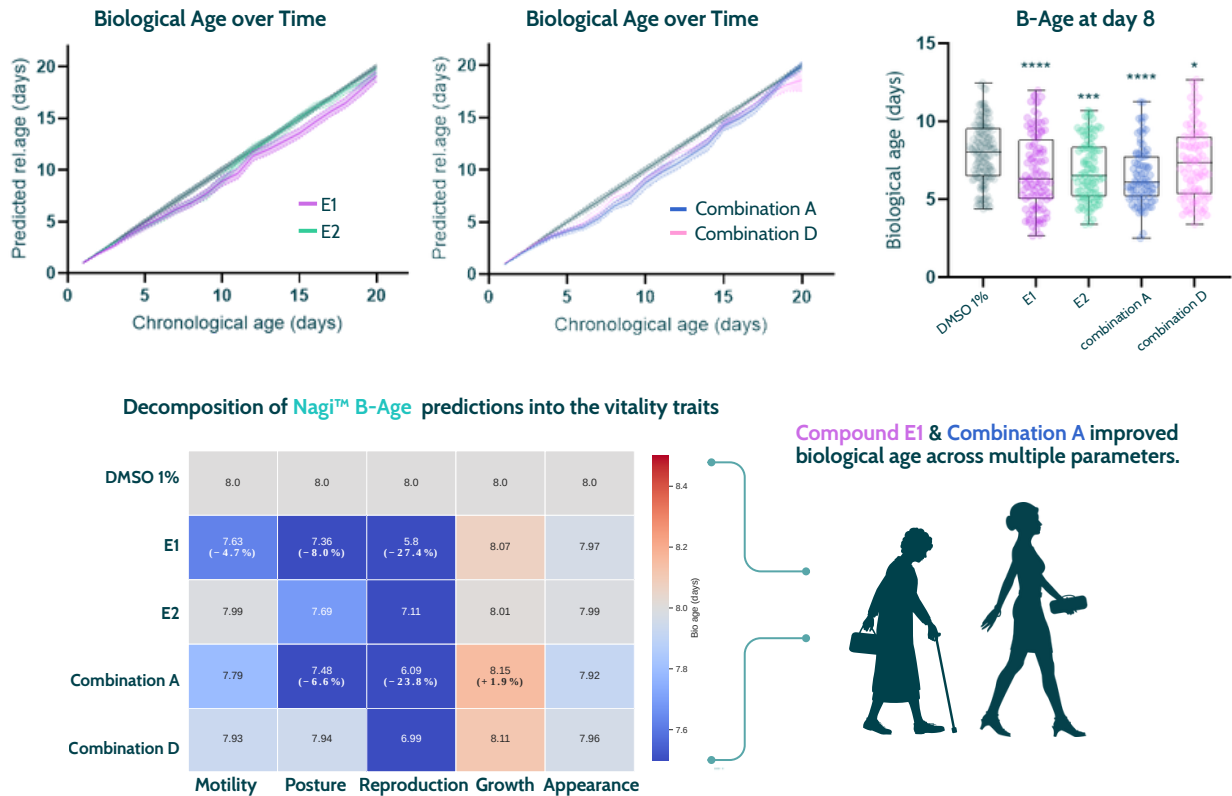


**Figure 3. Graphical representation of *C. elegans* reproduction (egg production) from L4 larvae injection until production of the first (left) and the last (middle) egg, as well as the average number of eggs laid per nematode within the timespan of egg laying (right).** Statistical analysis was performed using one-way ANOVA by comparing DMSO 1% with the treatment, followed by Bonferroni's multiple comparisons test. \* p<0.05

All tested conditions significantly reduced the number of laid eggs per organism when compared to the DMSO 1%. Additionally, the combination A treatment slightly impacted the time of the last laid egg, extending the overall timespan of egg laying. It's important to mention that interventions, such as caloric restriction, promote beneficial effects on longevity while reducing the ability to reproduce across species (1).

## Biological age measurement

Nagi™ B-Age allowed ElixIRA Pharma AG to pinpoint how their compounds individually and in combination influence the biological age, offering detailed insights into their mechanism of action.



**Figure 4: Evaluation of the effects of E1 and E2—individually and in combination—on *C. elegans* healthspan using Nagi™ B-Age.** Biological age prediction by Nagi™ B-Age, from day 0 to 20, for E1 & E2 and their combinations. A boxplot at day 8 illustrates differences in predicted biological age across conditions. Statistical significance was assessed with two-way ANOVA followed by Bonferroni's multiple comparisons test. \*  $p < 0.05$ . The Nagi™ B-Age prediction was further decomposed into individual vital traits. Significant changes in biological age, relative to the negative control, are expressed as percentage improvements or deteriorations. The overall change in biological age reflects the cumulative effect of changes across all vital traits.

By day 8, the biological age trajectories of the 4 different populations treated with E1, E2, and in combination (A & D) were distinct. A detailed analysis of the five vital traits revealed that the population treated with E1 compound and combination A showed lower biological age scores across multiple parameters (motility, posture, and reproduction), highlighting the sensitivity and predictive power of Nagi™ B-Age in identifying aging dynamics early in life.

Ready to transform  
your aging pipeline?

