

December 9, 2022

We appreciate the opportunity to comment on this most important strategic plan for ALS and for NINDS.

The process that brought us to fifteen priorities has been excellent. You have covered the spectrum of ALS research and you included a variety of representative stakeholders, including people living with ALS and caregivers. We are grateful.

We think that the priorities must be woven into a strategic plan that makes the whole greater than any individual priority. We are concerned that fifteen items are too many to each truly be priorities and strongly encourage consolidation and unification of the items, some of which overlap with others.

We suggest focusing on three foundational areas:

### **Diversity, equity, and inclusion**

Today US ALS clinical trials are concentrated in a few cities. The vast majority of people living with ALS simply don't have access to trials, and as a result, our ALS clinical research today does not reflect the actual population of people living with ALS. As the NIH has shown in other disease areas, substantially broadening the clinical trial network is essential and will not only give us more representative trial participation, it will also speed up trial enrollment significantly.

### **Information needs**

There are 17 mentions of "natural history" throughout the draft. The importance of biofluids is cited six times. There is a specific reference to the systematic gathering and sharing of patient data. We feel that a robust natural history study that reflects the actual ALS population better than any of the small studies of the past will be foundational to many of the other 14 priorities. This is a building block that will help multiple other priorities.

As attractive as the concept of data harmonization may be, it can also be an excuse for researchers to continue to work in their silos. A foundational, broad natural history study can help break down the silos.

As one Problem Solver with ALS said, "We need a 'come one come all' study." Such a study will give insights into the real population of people with ALS (as well as those at-risk genetically) and will better inform researchers of subgroups and biomarkers that are likely to accelerate their work substantially.

### **Leadership**

We believe NINDS must not underestimate the importance of its leadership to the success of this plan. Without it, these fifteen priorities are simply a wish list. We can't allow promising research to die on the vine, and we must be sure that the most promising aspects of the ALS portfolio are moving forward. They must be woven into a strategic plan that prioritizes the priorities. Foundational research must move ahead quickly. Opportunities must be seized. Duplication of efforts must be consolidated or eliminated. We look upon this as a constant activity for NINDS – much like an air-traffic controller who stays on alert and adjusts flight paths constantly.

Finally, thank you for mentioning the ALS Clock. We all need to assemble these priorities into a strategic plan that will move ALS research forward productively on that clock. If our overarching goal is to deliver treatments and cures for ALS on the ALS Clock, we need to make sure that the priorities are working **together**.

### **The ALS Problem Solvers**