Commentary on plasma p-tau217 subgroup analysis from Phase 2 Alzheimer's disease study

Good afternoon.

I hope you were able to join the webinar we conducted earlier today. This webinar reviewed SHINE data results we presented at the *Clinical Trials in Alzheimer's Disease*, or "CTAD" meeting. If you were unable to join us, a replay is available here.

What We Studied:

Yesterday we presented new analyses of how patients performed on CT1812 or placebo depending on the concentration of a protein called p-tau217. This protein is measured through blood tests. This analysis was pre-planned and built into the study design. The findings were presented in an oral session at the CTAD conference, and feedback from the scientists and clinicians at the conference was very positive.

Why We Studied p-Tau 217:

At the time we designed the SHINE study, there was a growing consensus that plasma p-tau217 was a sensitive marker of Alzheimer's disease biology. Another way to look at p-tau217 is as an indicator of neuronal damage in the brain. To study this we measured the p-tau level of all clinical trial participants and identified the median, which was 1.0pg/mL. We then compared cognitive scores in people with plasma levels above 1.0pg/mL versus those who were below 1.0.

Our Results:

We found that in multiple measures of cognition, **participants taking CT1812 with p-tau217 below the median did not lose any cognitive function over the 6-month study compared to people taking placebo. For these patients, cognitive loss was profoundly slowed for the duration of the study. By comparison, patients on placebo experienced a decline in cognitive function as their disease continued to progress.**

Why this Matters:

The study identified a group of patients who experienced a profound benefit from CT1812. This is the goal of every company researching effective therapies for AD. Importantly, for our clinical trials going forward, patients only need a blood test to determine their plasma p-tau level. This is an easy, convenient and low-cost approach to predicting who might benefit most from CT1812.

Our next step is to discuss these results and approaches to a Phase 3 development program with the FDA in an end-of-Phase 2 meeting.

Sincerely,

Lisa Ricciardi