By Richard Robinson

The ALS Association’s research program is specifically designed to discover and develop new therapies for ALS as quickly as possible. The structure of the research program has allowed The Association to take maximum advantage of the influx of new funding from the ALS Ice Bucket Challenge, according to Lucie Bruijn, Ph.D., M.B.A., Chief Scientist for The Association. Dr Bruijn provided an overview and update of the program and the latest discoveries in a recent webinar.

The research program, called TREAT ALS, is tightly focused on five key areas, Dr. Bruijn explained: gene discovery, development of disease models, drug development, biomarker discovery, and clinical studies. New genes lead to new models of the disease, which can reveal new ideas for therapy development, which are ultimately tested in clinical trials. “Central to all our programs are those who are living with the disease,” she said. Biomarker discovery is especially critical, she said, since they allow scientists to determine if a candidate drug is getting to its molecular target, and whether it is having its intended effect. With good biomarkers, even a failed treatment can teach researchers important lessons about ALS. Without them, a failed drug trial has little benefit for future research.

Through TREAT ALS, The Association funds academic-industry partnerships; provides infrastructure for multicenter clinical trials, especially through collaboration and funding of the Northeast ALS Consortium (NEALS); facilitates formation of international research consortia; and solicits and funds the most promising research ideas with grants to researchers. In the past 6 months, Dr. Bruijn said, the grant review team has reviewed more than 300 abstracts and has invited more than 200 research teams to submit more detailed research plans for consideration.

The Association is also working with the United States Food and Drug Administration on a “guidance document,” which will provide pharmaceutical companies valuable information on the FDA’s concerns regarding the design of clinical trials. This is meant to increase companies’ willingness to enter the risky pursuit of effective therapies for ALS by making it clear at the earliest stages how the trial should be structured.

“Ultimately, fundamental discoveries in ALS come from identifying new genes,” Dr. Bruijn said. To that end, The Association has funded major initiatives in gene discovery and pursuit of the disease mechanisms they trigger. Using ALS Ice Bucket Challenge donations, The Association has provided major funding for work by The New York Genome Center, Project MinE, the Neuro Collaborative, and Accelerated Therapeutics (ALS ACT), all ultimately designed to better
understand the disease and develop new therapies. People living with ALS can help by getting involved in clinical trials and donating tissue for important research. Details are available on the NEALS website: clinical trials: http://www.alsconsortium.org/trials.php and tissue donation: http://www.alsconsortium.org/donate_samples.php.

Among the most exciting new initiatives underway, Dr. Bruijn said, is a clinical trial, likely to begin next year, to test antisense therapy against the C9orf72 gene mutation, the most common genetic cause of ALS. Antisense therapy is designed to stop production of the harmful products of the gene. Much work is being done now to learn how best to measure the effects of the antisense treatment and to better understand how the mutation causes ALS.

Antisense therapy is one illustration of “precision medicine,” which is therapy targeted specifically at the cause of disease in the person receiving treatment. It is based on the growing recognition that there are multiple causes of ALS, and that the best treatment is likely to be the one that is focused on that primary cause. For instance, Dr. Bruijn noted, neuroinflammation may play a greater or lesser role in the disease of individual patients, and thus treatments against neuroinflammation may be more effective in some patients than in others. Biomarkers to detect this aspect of the disease, and the response to therapy against it, are critical for advancing such precision treatments. A test of such a therapy, with a biomarker component, is currently underway in partnership with ALS ACT and the company Neuraltus.

“Funding for the Milton Safenowitz Postdoctoral Fellowship program is also a key component of the research program,” Dr. Bruijn said. “It is very important to support young investigators, who are the future of ALS research.” New Fellows will be announced later this year.

Finally, Dr. Bruijn mentioned the new discovery, made possible with ALS Ice Bucket Challenge funds, of a previously unknown role for TDP-43, a protein found in abnormal aggregates in the motor neurons of most people with ALS. The work, by Philip Wong, Ph.D., and colleagues at Johns Hopkins University, showed that TDP-43 is responsible for suppressing the expression of certain portions of the genetic instructions, called “cryptic exons,” in order that the final protein product of the gene is properly formed. Aggregation of TDP-43 may prevent it from doing this job, leading to defective proteins and ultimately neuronal death. Dr. Wong will be the guest of an upcoming webinar to discuss his work.

“This is one example of how, through the ALS Ice Bucket Challenge, we have really been able to move opportunities forward in finding new treatments for ALS,” Dr. Bruijn said.