Telocyte Newsletter
Q3 2018

The major problem with innovation is that it is *innovative*. Incremental approaches to Alzheimer's intervention have – without exception – failed to slow disease progression. The field is ready for innovation, yet few people are able to evaluate innovative approaches with a clear eye toward the data, without preconceptions and without the conceptual blinders imposed by unexamined assumptions.

Everyone favors innovation, unless you are innovative.

Over the past two years, a number of pharmaceutical firms (and biotechnology companies) have not only encountered failure in their clinical trials but have decided to capitulate and abandon the search for an effective intervention for Alzheimer's disease. On the one hand, their pessimism is warranted: there have been more than 400 registered interventional Alzheimer's trials and no positive results. By itself, of course, this is surprising as statistical chance alone would be expected to result in better results than these, yet there it is. While poor clinical trial design may underlie many of the negative results, the primary problem is that these attempts are poorly aimed. Putting it bluntly, given that they have misunderstood the target, it is small wonder when they fail to hit it.

To adapt Coco Chanel's pithy advice – "*Don't spend time beating on a wall, hoping to transform it into a door*". To date, AD trials have made the classic blunder of beating their heads against the wall, rather than using the door.

The error lies in the unwillingness to reexamine their assumptions. Alois Alzheimer, for whom the disease was named more than a century ago, warned against the assumption that dementia was caused by the amyloid plaques and the other histological changes seen at autopsy. Despite his prescient advice, almost all trials have targeted amyloid, tau tangles, and other histological findings, never going deeper into the causes that underlie these findings. This is much like treating a fatal viral infection by treating pain, fever, hypotension, and other clinical findings rather than treating the virus itself. Every disease has its own signs and symptoms, but signs and symptoms are not a disease. Amyloid plaques, tau tangles, and mitochondrial dysfunction are outcomes, not causes. They are signs of the disease, even defining markers of the disease, but they are not underlying causes. So far, all clinical trials to date have only targeted disease markers.

Telocyte has a better idea.

Where we stand and where we are going

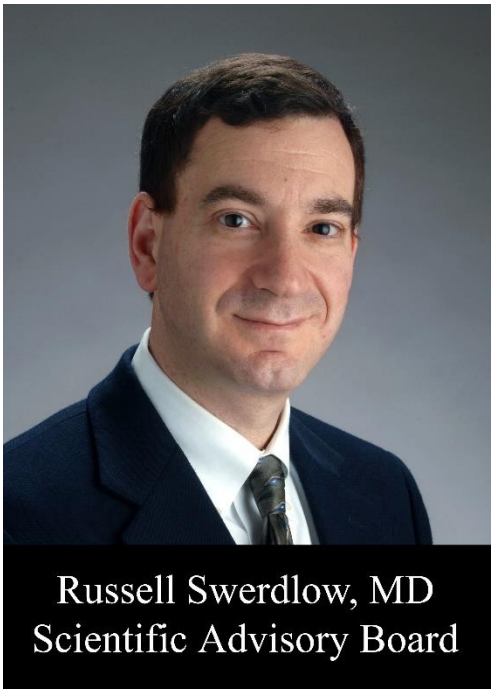
We have been offered the full support of a major global pharmaceutical investment firm. This investment will enable our phase 1 and phase 2 FDA human trials. We are now ready to apply to the FDA, to ensure that our protocols and production quality will meet the FDA expectations and requirements. In the next few months, we will finalize contracts for FDA consulting and for production of our telomerase gene therapy, TEL-01. Our timing now depends upon our ability to produce TEL-01 in sufficient quantity and quality to meet the needs of our

patients in the upcoming human trials. We have a growing patient registry of more than 100 volunteers for our FDA phase 1 human trial, currently scheduled to begin within the next two years.

We intend to ensure that TEL-01 is effective, safe, and credible.

Meet our Scientific Advisory Board:

Last quarter, we featured Dr. Mimoun Azzouz, one of our two world-renown specialists in gene therapy. We'd now like to introduce you an equally eminent neurologist and specialist in running Alzheimer's disease trials: Dr. Russell Swerdlow. Dr. Swerdlow has extensive experience in clinical medicine, human clinical trial design and execution, and FDA regulatory interactions in human Alzheimer's disease trials. In addition, we anticipate that Dr. Swerdlow will be our lead investigator for our FDA human trials.



Dr. Russell Swerdlow is the Director of the University of Kansas Alzheimer's Disease Center and the KUMC Neurodegenerative Disorders Program. Dr. Swerdlow is a Professor in the Departments of Neurology, Molecular and Integrative Physiology, and Biochemistry and Molecular Biology at the University of Kansas School of Medicine. After receiving his undergraduate and Doctor of Medicine degrees from New York University, he trained as a neurologist and cognitive disorders subspecialist at the University of Virginia. Dr. Swerdlow is a laboratory-based neuroscientist who is internationally known for his work on mitochondrial dysfunction in neurodegenerative diseases. National level recognition includes the S. Weir Mitchell Award from the American Academy of Neurology, a Cotzias Fellowship from the American Parkinson's Disease Association, research grants from the National Institutes of Health, and membership on NIH and Veteran's Administration Study Sections. Before joining KUMC in 2007, Dr. Swerdlow chaired the Alzheimer's Disease and Related Disorders Commission of the Commonwealth of Virginia, and from 2005-2010 he served as the Research Committee Chair for the CurePSP Foundation. His more than 200 scientific articles, focusing on Alzheimer's disease and mitochondrial function, have been published in *JAD* (Journal of Alzheimer's Disease), *Journal of Neurochemistry*, *Current Pharmaceutical Design*, *Biochim Biophys Acta*, *Human Molecular Genetics*, *PLoS ONE*, *Neurology*, *Experimental Neurology*, and other respected academic journals.