Telocyte Newsletter
Q3 2017

I often compare our progress to a three potential outcomes: the pessimistic, the optimistic, and the realistic. The pessimist outcome is failure, the optimistic outcome is miraculous, and the realistic outcome is the mean outcome for most biotech firms that make progress. If these were each placed on a scale from 0-10, then 0 is failure, 10 is a wildly miraculous outcome, and 5 is what happens to most successful biotech firms. Given this scale, we have been steadily progressing as a "6", i.e., better than we any realist would expect.

At the moment, we are in active negotiations with a global funding group that 1) sees and understands our aims and our understanding of age-related disease, 2) is excited about the clinical and commercial prospects, and 3) suggests funding us completely. While we ourselves are delighted, we will have to see what the negotiations bring over the next two months. We continue to talk with several other large investment groups, as well as individual investors. In the past month, I've been in Madrid, New York City, Palo Alto, and Montana, and am scheduled to be in London in a few weeks. The London trip not only includes several committee and personal meetings during the annual global Alzheimer's Association International Conference, but meetings with a member of parliament, a wealthy global investor, and various research groups in the UK.

On the FDA front, we have finalized our toxicity study protocol and are arranging an appointment with the FDA to ensure that this protocol meets their needs, as a prelude to our first human trial next year. While the FDA currently has a prolonged (several month) delay, we plan to begin the animal toxicity study in Q4 of this year, completing it in Q2 of 2018.

As discussed in our Q2 newsletter, while we continue to make contacts, have discussions, and encourage interactions with the FDA, academia, pharmaceutical groups, and other biotechnology firms, particularly those involved with Alzheimer's disease, we generally avoid publicity or headlines. We have given quite a few interviews regarding how Alzheimer's work and the prospects for an effective clinical intervention, but feel that our best "publicity" will be the results of our upcoming human trials, beginning in mid 2018.

The *Telocyte* patient registry

We often receive questions regarding human trials, currently scheduled for 2018. The location is not yet settled, but it will be held at an academic medical center in the United States, with the most likely suggestion being Kansas City. Treatment will be a one-time injection, with regular follow-up every two months, over a six month period. We will treat at least one dozen volunteers, each with moderately severe Alzheimer's disease and no other unstable medical problems. We currently have a registry of three dozen patients, one third of whom are less than 65 years old. If you would like to be added to the registry, please let us know.

Alzheimer's: a perspective

Many of us see media (as well as academic and biotech) updates on Alzheimer's on a daily basis. I typically find half a dozen come across my emails every day. Some of these stories offer hope, some increase our concern. Recently, Forbes offered an article suggesting that there were perhaps twice as many people with Alzheimer's as we had estimated, nationally and globally. In reality, there are not more people with Alzheimer's, but we've simply gotten a bit better at picking them up earlier (or so we think). With advances in imaging techniques, particularly targeted PET scans, we see earlier and earlier evidence of what will become Alzheimer's disease, often well before it is clinically apparent. Until recently, the diagnosis was made solely on clinical grounds: you were having more and more memory or cognitive problems, you were tested and interviewed, and you were diagnosed with Alzheimer's, solely on clinical grounds Purists continued to maintain that only an autopsy justified a firm diagnosis, but the reality was that clinical diagnosis was acceptable and accepted.

More recently, however, we've begun to use not only CT and MRI scans to detect anatomic changes in the brain, but PET scans, which can focus on actual metabolic function (rather than just anatomy), so we began to see not only which areas of the brain had loss of neurons, but which areas had neurons that were still there, but were already "in trouble". PET scans also allow us to look at even minimal changes in amyloid and tau proteins, changes that predict upcoming neuron failure and clinical Alzheimer's disease.

This is a diagnostic two-edged sword. On the one hand, it offers to tell you that, while you don't yet have Alzheimer's, you soon will. Is this bad news or good news? Is ignorance bliss or a chance to make plans?

This is also a therapeutic two-edged sword. On the one hand, we might be able to "catch it earlier" and begin early therapy. On the other hand, there is no therapy that has yet proven capable of changing the course of the disease, whether you catch it earlier or not.

In short, the recent advances don't really change the human tragedy of AD at all.

We are slightly better at diagnosing AD, but no better at treating it. Most global pharmaceutical firms and most biotech firms are focused on testing their interventions on early Alzheimer's disease and are, frankly, having a hard time finding enough patients. Their rationale for going after early disease is clear: the earlier you start treating it, the better the chance of slowing it down. Unstated, however, is the clear assumption that none of these companies want to treat moderate AD because none of them believe that AD can be stopped, let alone reversed. They are hoping that they can "stop the avalanche before it gets started" or, more realistically, find a way to slow the inevitable downhill course, at least marginally, Stopping AD or curing AD are no longer part of reality for most companies.

Oddly enough, that's precisely where Telocyte comes in. We are the only company that will be treating patients with moderate (rather than early) Alzheimer's. We are also the only company that is confident that we can both prevent and cure (rather than merely slow or postpone) Alzheimer's.

It's a dizzying perspective.