Telocyte Newsletter
Q3 2019

In our Q1 2017 newsletter, as CEO, I wrote about the reasons why I co-founded Telocyte with Michael; today I reflect on our progress, learning and challenges over the last 2 years. Back then, we contributed and participated in the very first Advanced Therapy Medicinal Products (ATMP) conference in London, UK. It was our first presentation as Telocyte, introducing our telomerase gene therapy which resulted in our contribution to the Advanced Therapies Investment Report 2017.

For me, it was an opportunity to access this emergent advanced therapy sector and industry in terms of its maturity and acceptance. Unsurprisingly, it was characterised predominantly by small, young biotechnology companies developing therapeutic agents and peripheral technologies, supported largely by academic and publicly funded basic and translational research efforts.

There were a few of the large pharmaceutical folks but the subsequent discussion panels were largely downbeat focusing predominantly on the manufacturing commercial operations and supply chain challenges; as well as building value for Cell and Gene Therapies and establishing Market Access pathways. The Editor's opening paragraph of the report nicely summarised the arc of medical successes but pointed to the elephant in the room (my emphasis).

> *The past 60 years have seen globally significant advances in medical technology which have drastically increased both quality and expectancy of life across the globe. Made possible through advancements in antibiotics, vaccinations, small molecule drugs, and biologics, the developed world now expects to live long and healthy lives. Successes in medical science have supressed the incidence of predominantly acute external pathologies, altering the clinical landscape to place chronic internal failures of the body firmly in the foreground. 80% of 2012 EU deaths were a result of non-communicable diseases. Despite on-going and partially successful efforts from existing treatment modalities, heart failure and cancer together account for over a million deaths every year in the US, and in the EU, there are an estimated 1.3 million annual deaths from cancer alone. Progress in cancer treatment has been slow; treatment approaches have remained largely unchanged since chemotherapy became commonplace in the 1940s, and often, cancer treatment side effects can be as damaging as the disease itself.*

What was most shocking to me about this statement was that deaths from Alzheimer's Disease were not even mentioned or on the radar screen. In November 2017, the news broke: "Dementia now Britain's biggest killer overtaking heart disease for the first time" with dire predictions suggesting that 1.2 million people would be

living with dementia by 2040. According to the Alzheimer's Association 2018 Alzheimer's Disease Facts and Figures report, an estimated 5.7 million Americans of all ages were living with Alzheimer's dementia. They went on to say:

> *By 2025, the number of people age 65 and older with Alzheimer's dementia is projected to reach 7.1 million – almost a 29 percent increase from the 5.5 million age 65 and older affected in 2018. By 2050, the number of people age 65 and older with Alzheimer's dementia may grow from 5.5 million to a projected 13.8 million, barring the development of medical breakthroughs to prevent, slow, or cure Alzheimer's disease.*

As 2017 progressed, it was clear Telocyte would need to establish a detailed program plan and clinical protocol for our telomerase gene therapy approach to treating Alzheimer's Disease, a plan that we could confidently share with potential investors and of course the FDA, detailing budgets, manufacturing and quality compliance, toxicity study and clinical protocols. Our first investor has allowed us to do just that by working with our excellent Scientific Advisory Board, PPD (our CRO), and Cooley LLP (our legal team). This was a non-trivial effort, but I can report we are now ready to move forward into our Phase 1 program.

From day one, Telocyte has been a company with a global outlook. One of our first actions was to establish a website to provide information to both those families with Alzheimer's Disease to understand our approach and our progress but also to investors who wanted to know more about Telocyte and the team.

This has attracted attention from around the world and we are today in discussions with investor groups from the US, EU and China. Selecting and working with the right investor is critically important to us and so education and due diligence discussions on both sides are taking up a lot of our time. When asked by families of Alzheimer's patients why it is taking so long to for us to commence clinical trials, this is a large part of the reason.

Another frequent question we get asked is; why are there no treatments, after all the research time and billions of dollars expended by charities and large pharmaceutical companies? Telocyte has chosen large molecule biologics to address Alzheimer's disease using a therapeutic gene. Previous attempts from pharmaceutical biotech companies to provide an effective clinical intervention for Alzheimer's have failed because these companies chose the wrong technology and targeted disease symptoms, rather than the root cause, using a classical small molecule, chemical approach. The halting of late stage drug trials by *Roche* and *Biogen/ESAI* are the most recent examples of this failed approach.

Since 2017, our experience has been that a number of investors and academics believed that biologics (and Telocyte) were not relevant, as there were several major pharmaceutical companies that were already progressing with drug trials to address Alzheimer's. They felt that such trials were making good progress and were clearly going to result in an effective clinical intervention. The science emanating from major universities and research laboratories agreed that the only viable drug targets – using small molecular drugs – were beta amyloid or tau tangles. This was an accepted consensus.

Large pharmaceutical companies are fully geared up to engineer small molecule chemical structures that can be deployed and then biologically evaluated for efficacy and safety. It is a time-consuming and very expensive process, consuming hundreds of millions of dollars over many years. Unfortunately for them (and for those with Alzheimer's disease) they failed. We predicted exactly that, although we take no pleasure being proven right. Time, money, and lives have been needlessly wasted. As Albert Einstein was said to have commented, "*Insanity: doing the same thing over and over again and expecting different results.*"

If you have been following our quarterly newsletters, you will have seen that we have a very different view regarding the pathology of Alzheimer's based on the work of Dr Michael Fossel, my colleague and co-founder. Our position for taking a **biologics** approach is clear:

> *"The cell senescence model of age-related disease provides a single framework for understanding many age-related diseases, specifically including the dementias, such as Alzheimer's disease. It further suggests that such diseases may be both prevented and effectively treated through a gene-therapy intervention that is currently feasible and that would effectively test the cell senescence model "*

Reality is the forcing function for change. The twenty-first century is facing new realities on many fronts; from coping with science technology developments arriving at exponential speed, to dealing with global plastic pollution and temperature rise with subsequent climate changes and (of course) the rapidly expanding incidence of age-related diseases like Alzheimer's. Telocyte is responding to that exponential growth in age-related disease, as we live longer and more of us age. When looking at our '*Healthspan*' as opposed to our '*Lifespan'* we see that our last decades are blighted, as we suffer the insults of aging. Unsurprisingly, this outcome has been universally accepted as natural and, despite various claims for clinical interventions, the care and support to mitigate aging and age-related disease has been disappointing.

Telocyte has a different approach, based on deeper insight and a recognition of a new horizon for healthcare. This week, we could not agree more with the announcements coming from Cambridge University, at the Health Horizons Future Healthcare Forum:

> "*Over the previous 20 years we have seen a significant change in the healthcare industry. Small molecules have been pushed out of the blockbuster limelight by biologics. Decreasing sequencing cost has allowed more targeted R&D and the use of increasingly interdisciplinary data to influence prognosis has become standard practice*."

As I said in 2017, Telocyte was founded to rapidly bring telomerase gene therapy to first clinical human trials for Alzheimer's Disease. Our strategic objectives remain clear:

- We will measure our success by curing patients.
- We will provide proven clinical interventions.

- We will provide cures for age-related diseases.

At Telocyte, we are contrarians, swimming against a consensus view, but we have good reasons, good data, and a clear view of the real point of intervention in the cascade of pathology that is age-related disease. Our focus is on the generation suffering **today** with Alzheimer's Disease, not 20 years from now. We are looking forward to an exciting future for them and for us!