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Targeting the Mechanisms of Aging, Repair Biotechnologies is developing Damage Repair Therapies Capable of producing Meaningful Rejuvenation

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CEOCFO: ***According to the Repair Biotechnologies site, your mission is to "improve human healthspan." Just briefly, what is your approach?***

Reason: Targeting the mechanisms of aging is an important approach to the treatment of aging as a medical condition, well proven in animal studies for decades now. Aging as we observe it is simply an accumulation of cell and tissue damage and its downstream consequences: the way forward is to either repair the damage or block the earliest and most consequences. Yet the research and medical development communities have largely ignored this strategy in favor of the much worse approach of trying to paper over the very complicated later stages of aging, when damage has spread into a poorly understood mess of disrupted metabolism.

Why this is the case is a much longer topic for discussion, but what it means in practice is that the research community is littered with promising biotechnologies targeting the causative mechanisms of aging that have yet to be carried forward. One just has to know where to look, and be guided be a suitable philosophy of development – damage repair in our case. At Repair Biotechnologies, we pick the best of the low hanging fruit likely to result in significant repair or reversal of cell and tissue damage and carry it forward towards the clinic.

CEOCFO: ***Why/how did you personally develop an interest in aging?***

Reason: Utilitarian selfish altruism; we see the results of degenerative aging all around us, the pain, the suffering, the death. I've no great desire to find myself in that situation, nor any great desire to see everyone else in that situation. After that, it is just a matter of finding out what can be done about it.

Rationally, it is clearly the case that aging is by far the greatest cause of suffering, death, and cost to humanity. It outweighs the next nearest single cause by a very large factor. Yet the cost of developing effective therapies to address causes of aging, repairing the damage, given the present state of scientific knowledge, is no greater than that already being spent on (largely futile or low yield) approaches to papering over late-stage consequences of cardiovascular disease or Alzheimer's disease. If one wants to change the world for the better, then building therapies that treat the root cause mechanisms of aging is the best opportunity by far when it comes to cost versus benefit.

CEOCFO: ***How do you decide what parts of the aging process to consider?***

Reason: The SENS (Strategies for Engineered Negligible Senescence) roadmap is very influential on our thinking. There are good and bad ways to try to treat aging and aging-related disease. The past century is more or less a catalog of all of the bad ways: trying to treat the symptoms rather than the causes; trying to mimic the slowing of aging observed in calorie restriction; trying to find out why centenarians live longer and mimic that; and so on.

We think that the present stunning successes in animal studies of senolytic therapies that selectively destroy senescent cells is a strong validation of the SENS roadmap. That was advocated in SENS in 2002 and earlier, and rejected by most of the rest of the aging research community until 2011 or so, when someone finally managed to raise the funding to prove that it worked very, very well in mice. The present human trials of senolytics will be rolling out what should be compelling results over the next year or two.

Senolytics is just one of a range of approaches to repair of damage. When looking for projects, one mixes the top down approach with the bottom up approach. Top down, one looks at a SENS category, and surveys the research community to see who is working on something interesting that is close to realization. Bottom up, one surveys the research community to see what catches the eye, and then decide whether or not the work represents a form of damage repair.

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CEOCFO: ***What are you looking at now and what do you hope to find?***

Reason: At present, our first two projects focus on restoration of the thymus and reversal of atherosclerosis.

The thymus is where immune cells of the adaptive immune system mature after their creation in the bone marrow. Unfortunately, its active tissue is replaced with fat over the course of later life, and the consequent reduction in supply of immune cells is one very important determinant of immune aging. The immune system, lacking new reinforcements and replacements, becomes cluttered with damaged, useless, and actively harmful cells. It becomes simultaneously overactive and inflammatory but also incompetent. A lot of light and noise, but no benefit: in fact, this is enormously disruptive to tissue function throughout the body. We hope that regenerating the thymus and thus restoring the supply of immune cells will fix a large fraction of this problem.

Atherosclerosis is one of the most significant single causes of death, perhaps a sixth of everyone by some counts. Fatty plaques build up in blood vessel walls, narrowing and weakening them. Eventually something important ruptures, with fatal consequences. The present treatments are near all based on reducing cholesterol in the bloodstream, which only slows the process down by reducing the input of cholesterol into plaque-forming mechanisms. It cannot greatly reverse existing plaques and it doesn't block the mechanisms responsible for adding to those plaques – it just gives them a little more breathing room. That isn't enough. To our eyes the right way to go is to make the cells and mechanisms responsible for cleaning out cholesterol from blood vessel walls much more resilient or more effective. The condition occurs because of age-related disruption to the activities of these cells and their efforts, such as resulting from the presence of oxidized cholesterol. If cells can be made immune to this sort of harm, then in principle plaques will never form in the first place. We are presently testing this approach in animal studies.

CEOCFO: ***How does your approach compare to other research in aging?***

Reason: Sadly, the approach of repairing damage is still something of a minority concern in the research community. It remains the case that most research follows the pattern of (a) examine the late stage disease state, (b) work backwards to find the first interesting proximate cause, (c) be pressured by the institution to find some commercial use for the research, (d) someone starts a development program based on intervening at the proximate cause.

This is a recipe for expensive, marginal therapies that have limited utility and a tendency to fail at Phase III clinical trials. The entire regulatory framework for medical development is arguably set up to distinguish slightly better marginal, unreliable therapies from slightly worse marginal, unreliable therapies. Intervening in a later stage of damage and complex interactions in a complex system is always going to be worse than intervening earlier at the level of root causes.

Consider rust in an ornate, complex metal scaffold. Do you send people in to model how it will fall apart, prop it up, and weld as portions fail in unexpected ways, or just rust proof it every few years? Rust is a very simple process. The way in which a metal scaffold fails due to rust is only limited in complexity by the complexity of the scaffold itself. This analogy holds up very well in the matter of aging: simpler causes produce complex outcomes because we are complex biological systems. Intervening at the level of the simpler causes will always be easier and more cost effective.

CEOCFO: ***Would you tell us how the recent funds from your seed round will be used?***

Reason: We will be moving our thymus regeneration program to readiness our first meeting with the FDA. This means the usual work of settling on the final formulation of the therapeutic, putting together a supporting package of animal model data, planning out and documenting our GMP manufacture, and so forth.

CEOCFO: ***How long will the funds last?***

Reason: Actually far past the point at which we'll be raising our next round. We're quite securely funded for our planned development path.

CEOCFO: ***What does the next year look like for Repair Biotechnologies?***

Reason: We'll finalize our entry to the IND process for our thymus regeneration program, as well as continuing the lengthier animal studies required to prove out our technology for reversal of atherosclerotic plaques. We are assessing a range of other potential damage repair programs and funding sources, and expect to expand our pipeline over the course of 2019 and 2020.

CEOCFO: ***Why should Repair Biotechnologies standout to both the healthcare and investment communities?***

Reason: We are representative of a growing number of companies in the new and rapidly growing rejuvenation industry, all working on ways to treat the causes of age-related disease rather than papering over the symptoms. It is a new and far better approach to medicine for age-related conditions, offering the possibility to greatly and reliably increase human healthspan, to prevent and reverse age-related disease to a degree that could only be hoped for until this present time. The ultimate market size is truly enormous: every human being much over the age of 40 is a potential repeat customer for damage repair therapies capable of producing meaningful rejuvenation at some price point.