



INVESTMENT STRATEGY UPDATE

March 31, 2017

ANTI-AGING AND VITALITY

“The future ain’t what it used to be.” – Yogi Berra

From time immemorial, mankind has been searching for ways to live longer and more vital lives. Ponce de Leon’s mythical search for the fountain of youth may have been a fool’s errand, but what is the outlook now, given the incredible recent advances in computing power and in our understanding of how the human body functions? For a species that has found it easier to map a genome than the ocean floor, will big answers come from the smallest aspects of physical being? And from BTR’s perspective, what are the investment implications? This quarter’s *Investment Strategy Update* explores the question of whether discovering the secrets to longer, healthier lives is within the grasp of companies and technologies that already exist.

What We Are Learning

According to the World Health Organization, in 1900 the average life expectancy in wealthy countries was 50 years, while on a global basis it was only 31. By 1950, the global average had moved up to 48 years, and by 2014 it was estimated to be above 70. Notably, these numbers are from birth, whereas the current life expectancy of a 65 year old is another 20 years. Most researchers believe the maximum possible lifespan to be around 120 years. Highly interrelated and probably more important is the concept of “healthspan” (i.e. vitality or youthfulness). Most people if asked would probably agree that their goal would be not merely to live a long life, but to have a high quality of life for as long as possible.

What we know is that aging itself is the major risk factor of death from all chronic diseases, including heart disease, cancer, stroke, diabetes, kidney disease, osteoporosis, Parkinson’s, and Alzheimer’s (not to mention plain old accidents). The risk of getting any of these conditions multiplies exponentially with age. Contracting one or more of these will not only shorten one’s lifespan, but clearly negatively impact one’s vitality as well. If it were possible to slow down the aging process, it would be possible to postpone chronic diseases.

In theory, we all know the prosaic steps we should take in order to live a longer, more vital life: eat vegetables, get a good night’s sleep, exercise regularly. Ongoing research continues to refine this sound advice, such as the USDA replacing the “food pyramid” chart several years ago with a differently balanced chart that de-emphasizes the intake of carbohydrates. Researchers have also determined that quality sleep in the range of seven to eight hours is required to recharge the body and reduce the level of stress hormones. Interestingly, more than eight hours appears to be less optimal for longevity. On the exercise front, a large and growing body of research shows that intensity level is more important than overall amount. It may only take ten to twenty minutes of vigorous (i.e. uncomfortable) exercise per week

to increase vitality and lengthen lifespan, whereas several hours of lower intensity exercise might not do as much good. Using mice that were bred to age rapidly, researchers exercised one group at high intensities and another identical group at an easier aerobic level. The high intensity group stayed much more vital while the low aerobic group turned grey and lost muscle mass. It also appears that lifting heavier weights keeps you more vital than lifting lighter weights.

What Potential Solutions Are Currently Available

Pharmaceutical research continues to explore novel compounds, even though there is no current regulatory pathway, as the FDA does not consider aging a disease. There are, however, several existing drugs approved for other indications that are already on the market and appear to have the positive side effects of increasing longevity and vitality. Metformin, a decades-old and pennies-per-day generic drug prescribed for Type 2 diabetes, clearly extends the life and health of those afflicted with high blood sugar and also appears to decrease the incidence of cancer. What is particularly interesting is that in a recent large population-based study, older Type 2 diabetics on Metformin lived longer than the similar non-diabetic control group not taking Metformin. Normally an aging Type 2 diabetic population would be expected to die several years earlier than those not afflicted. Could Metformin also be an anti-aging drug for older people without diabetes? There are clinical studies proposed to answer that very question.

Several different animal trials have shown that severely calorie-restricted diets increase lifespans. We are pretty sure most people would balk at being urged to eat 33% fewer calories than normal for the rest of their now longer lives, so researchers are looking for ways to achieve the benefits of a so-called starvation diet. An existing drug called Rapamycin, which is used to prevent organ rejection in transplant patients, appears to mimic starvation, but it will take multiple years of research and trials before this might actually be prescribed as a longevity drug.

Statins are drugs used to control high cholesterol, and which have significantly extended the life expectancy of those with heart disease. Many of these statins are generic and cost only cents per day. Additionally, new and more precise lab tests are now able to detect unhealthy levels of cholesterol particles even when overall cholesterol appears normal. By avoiding damage to the heart and/or major surgery, patients should be expected to increase healthspan as well.

Through the ages, many cases of poor health and shortened lifespans have been the result of simple nutritional deficiencies. Scurvy, caused by a lack of vitamin C, readily comes to mind. While most experts agree that it's best to get the majority of our nutrients from the food we eat, there is still a huge market in the U.S. for supplements, though it is much less regulated than pharmaceuticals, and more prone to hype. There is interesting ongoing clinical research with various forms of vitamin B3 that shows promise of making cells and their mitochondria (the part of the cell responsible for energy production) more youthful in older subjects. Time will tell whether there is a real longevity or vitality benefit from some of these compounds or whether they merely turn out to be a batch of snake oil.

In high-end concierge medicine, it is possible to completely sequence one's own DNA, and then compare the results with a growing database of DNA correlated with medical records. This expensive process will become more available as computing power and data storage continue to decrease in price. With this information, it is possible to determine one's genetic predisposition to certain afflictions, and take appropriate actions earlier. Another area where costs are coming down and technology is catching up with previous promise is with high-resolution magnetic resonance imaging of the entire body. The promise here is that cancer cells show up differently than normal cells on such scans, and therefore cancers can be detected earlier, when more and better treatment options are available.

Alas, even as our knowledge increases dramatically, costs come down rapidly, and real options become available, history would suggest that only a small percentage of our population will take advantage of the possibilities. One merely need look at smoking as an example. It is almost universally understood that smoking lowers lifespans and decreases healthspan. Yet according to the Centers for Disease Control, currently more than one out of every seven U.S. adults smokes. It is also widely known that obesity is highly correlated with poor health. Nevertheless, the National Institutes of Health report that 35% of the U.S. population is obese and another 7% are morbidly obese, in large part due to poor eating habits and lack of exercise.

Investment Implications

Clearly, if a lab was able to patent a "fountain of youth" pill, the world would beat a path to its doorstep. Some of this research is being done in the larger pharmaceutical firms, but given the size of these companies, any new drugs would have to be real blockbusters to have a meaningful effect on stock price. There are a large number of smaller and riskier companies doing cutting edge research as well, and we think the best way to invest in them is through a large basket of small companies.

Ironically, the real breakthroughs in life-improving pharmaceuticals or other treatments may not ultimately come from a traditional health care company, but rather from a technology company; or at least, as a result of the "big data" such companies are gathering and the analytical skills or even artificial intelligence that can be applied to it.

Monitoring devices and applications are improving rapidly to the point where the elderly can be checked on and reminded to take medications remotely. We think smart watches and other small devices will become even more sophisticated and useful over time, while smart phones and robust wireless networks will play an integral part in the communication of this data. Yet another manifestation of the Internet of Things.

As lifespans continue to expand, we see an increased demand for replacement parts. The poster child for this trend is hip replacement, where post-operation satisfaction is now around 95%. We also believe lab cultivation (or even three-dimensional printing) of human replacement organs will become a reality in the not-too-distant future.

There are a host of beneficiaries if more people live longer, healthier lives. Assuming this trend goes hand-in-hand with extended earning years, recreation and travel sectors would see increased demand, as the older demographic spends more on discretionary items and less on remedial or emergency health care. On the other hand, life insurance, annuities, and retirement products will have to be rethought as life expectancies increase.

In the shorter-run, we believe that there will be a continued need to invest in and support a significant not-so-vital aging population. Particular areas of interest will include nursing homes and assisted living facilities. Driverless cars could also provide a large benefit to this population, as well as to the rest of society's drivers, bicyclists, and pedestrians.

Market Outlook

From November's Presidential election until very recently, the stock market had moved up in an almost uninterrupted fashion. Optimism about economic growth stemming from lower tax rates, reduced regulation, and other forms of fiscal stimulus drove economically sensitive stocks to all-time highs. We could currently be experiencing the start of a correction within that process, and it remains to be seen how deep it will be. To the extent it is just drama surrounding the President being used as an excuse to take profits, we expect the process to be quick. To the extent it represents real concern that his legislative agenda will stall or be stymied completely, it could take longer and go lower. In either case, we view it all as normal and healthy. And though we believe there would be benefits from tax reform, the reversal of certain onerous regulations, and increased infrastructure spending, the status quo, as it relates to the stock market, would still be quite good. In fact, we are concerned that increased fiscal stimulus, if not done right, could lead more to inflation than to economic and earnings growth, which would force the Fed to raise interest rates more quickly than it would otherwise like, potentially pulling the next recession forward in time.

The Fed, for its part, has made it clear it will continue to raise short-term interest rates at a modest pace. After peaking at approximately 2.6% on the benchmark 10-year U.S. Treasury note just before the March Fed Governors meeting, bond rates have started to come down. We try to use interest rate spikes as opportunities to buy bonds and increase average maturities, and we do not currently believe that the trajectory of rates is all that steep. We are mindful of whether the yield curve could flatten further. Whether it does or not will inform our decisions not only on bonds, but also on interest rate-sensitive stocks.

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