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Life Length

was founded through the CNIO (Spanish National Cancer Research Center) combined with the support of the Botín Foundation, Matlin Associates and Dr. Maria Blasco's work in telomeres. Stephen J. Matlin, CEO of Life Length, discusses the potential of the company's diagnostic test to become a standard biomarker for biological age and for age-related diseases.

What is the potential of CNIO and similar institutes in Spain to produce similar, commercially viable companies like Life Length?

Spain has never been in the same league as other developed countries for biotech and pharma development, partially because there has never been a giant Spanish pharmaceutical company. In fact, Spain is the only big European country that does not have its own global pharma company. Global companies are critical to and often responsible for creating spinoffs. Academically speaking, the Spanish government must truly commit to investing in sustained R&D. The Spanish National Cancer Research Center (CNIO) is the premier research institution in Spain, and the only one routinely listed among the top ten in cancer research worldwide. It is a real fight to stay on that list; CNIO's annual budget is about €50 million, whereas other institutes of equal quality like MD Anderson have annual budgets of $2 billion.

As medicine moves into the world of genetics, the human genome and seeks to address tremendously complex diseases, the pharma industry will continue to consolidate because the scale needed to be relevant is huge. I hope the Spanish government will continue to support and fund such institutions so that they can actually develop novel research that can eventually be translated to the marketplace. Furthermore, even with great science, you still need an entrepreneurial ecosystem around the scientists, which Spain historically has lacked. Looking at the number of papers published versus the number of patents made and number of companies created, the slope of that angle is always downward but less so in the US versus Spain where it is steep. There is a lot of very solid science here that never sees the light of day. In the US or UK, potential technology or new discoveries are quickly presented to venture capital groups or businesspeople, so the time to market is faster and fewer opportunities are lost.. Spain needs to continue to develop that ecosystem of taking ideas and discoveries from the lab to a company, universities' tech transfer departments who work with scientists to register patents, or the pharma industry. As an example, MIT wanted to introduce Life Length to their corporate partners; we need more of this activity in Spain. I hope Life Length can be a good case study for other companies, government and policymakers to see how that could happen.

Do you think that globalization has given the Spanish the opportunity to reverse this trend?

They can embrace it more, but the entrepreneurial gene is simply not as common in Spain. But perhaps more importantly, it is very challenging to start up a company in Spain. Firstly, the market is much smaller. An American company can become worth billions of dollars without ever leaving the US, so by the time that company goes international, it is already a success. In a small country like Spain, your domestic market limits your ability to get to scale and be competitive; therefore Spanish companies must be international from the beginning. We knew from day one that our activity, as a very specialized diagnostic testing services firm, would initially not have a broad enough appeal to the mass market to have a big business in Spain.

Second, Spanish people also need a more supportive environment in which tenacity and risk-taking is encouraged by the Spanish government and society, one in which failure is perceived as acceptable. Additionally, Spain's highly bureaucratic nature often impedes progress. Life Length was fortunate to have greater financial and institutional muscle and political capital compared to other companies thanks to the Botín Foundation, as well as the prestige of being spun-off from the CNIO.

The study of telomeres and telomerase is relatively new. What is the global interest in this subject as a scope for commerce?

Before we started Life Length, we spent over a year doing very careful market research to effectively look at this very issue. This incredibly powerful technology which we call Telomere Analysis Technology® (TAT®) measures telomeres, found on the tips of chromosomes, and we initially thought there would be a market for this in two areas. One was a tool for academic research, such as scientists and doctors investigating whether there is a causal relationship between telomere loss and telomere attrition and disease. The second was a tool for industry as a companion biomarker in current and developing products to determine whether drugs, nutraceuticals, vitamins, active ingredients in creams and cosmetics, or even how food affects the rate of ageing as expressed by telomere attrition and rate of loss.

To provide context for the second market example, 85 to 90 percent of all adult cancers escape the limit that causes cells to become senescent because they endogenously express telomerase (the enzyme that repairs telomeres whose discovery was the 2009 Nobel Prize in Medicine), allowing them to continually divide and metastasize rapidly, essentially meaning that every cell in that tumor is immortal. If a pharmaceutical company were able inhibit the expression of telomerase in those cells, this could potentially be a blockbuster drug that addresses almost all human cancer. Pharmaceutical companies now need to figure out how to deliver such a target with a technology that measures whether your potential molecules can slow telomerase expression, which means screening compounds. Life Length offers that testing service to the industry.

Other examples include characterization of cell therapy and regenerative medicine products where our technology is providing a much needed quality control tool and services to nutraceutical or pharmaceutical companies that want to show that their drug, supplement or even yoghurt may slow or reverse the loss of telomere, reverting the ageing process. This makes our technology relevant for many sectors.

The third market area that we originally did not anticipate is that society is fascinated with this technology’s concept. It is understandable; everybody wants to age as gracefully and as healthily as possible. The idea of biological age as expressed by this genetic biomarker, which is a very precise and objective measurement of the ageing process, is very appealing to physicians and patients worldwide. Culturally, everybody has the same interest in health. We have seen a global demand from physicians who want to adopt our test as an innovative biomarker of health.

What is the global academic interest in telomeres for researching this life-changing technology?

There are more than 17,000 peer-reviewed papers published on telomere biology and its relationship to just about any disease. For example, in cardiology there are more than 600 publications that show that short telomeres correlate to higher cardiovascular risk and death from CVD. Patients in the first quartile of the shortest telomeres may have eight times the risk of dying from heart attacks. Consequently, Life Length is beginning to work with cardiologists who use our test as a companion biomarker to provide a richer insight in terms of a predicative and measure of disease and to take proactive, preventive action.

Life Length's diagnostic is also ten times more precise than similar products. How was this technology developed?

The technology started in the laboratory of Dr. Blasco, one of the world's leading scientists in telomere biology. Essentially, existing technologies used to measure telomeres are actually semi-quantitative, often imprecise, and dependent on lab technicians' experience. Dr. Blasco discovered a way to use a technique called Q-FISH (Quantitative Fluorescent *in situ* Hybridization), which allows you to look at measure telomere individually. After five years and approximately €20 million invested in research, technical studies and development, we realized this really was a quantitative and qualitative step forward over current technology. In late 2010, the Botín Foundation, the Spanish government and I put together a company that would license the technology from the CNIO to which we would pay royalties, generating a return for Spanish society. Since then, the technology has evolved dramatically as we have industrialized and scaled it for commercial use.

Has this technology's capacity to measure the toxicity of drugs created a sense of cautiousness among pharmaceutical companies, whose drugs may in fact lead to faster telomere loss?

A Phase I trial is essentially a series of dozens or even hundreds of tests for toxicity, all of which must be passed before moving to Phase II. Historically, telomere testing has not been part of that because no technology previously existed that allowed industry to observe it. As an example, nobody really knows if aspirin harms us in terms of telomere loss because that study has never been done. Such a study might indicate that aspirin may support or may hinder the ability to express low levels of telomerase, decreasing or increasing the rate of ageing in the heart. In any case, the introduction of new biomarkers and assays are coming regardless, all of which will become standard screening tools, compelling the entire industry to follow suit. However, it is

important to note that we want to work with industry rather than become a regulatory barrier, and believe that our technology can be very insightful for them.

Apart from working with academia and industry, what is the global commercial strategy to sell this technology to physicians or the general public?

When Life Length started gaining some visibility, the attraction skyrocketed. We were featured on the cover of several newspapers around the world and were visited by a number by BBC; CNN and other major media, and this had never happened in the history of Spanish biotech startups and is unusual for any small company. The concept of biological age has always been around, but Life Length has a scientific and objective basis that can be correlated to this biomarker of telomeres. As a result of this media exposure, we received many thousands of e-mails from countries around the world from people wanting to measure their telomeres; individuals, physicians and institutions and corporate clients. In order to get samples from all corners of the globe to Madrid we started working with big diagnostic labs in each country, who became local partners that transferred blood samples from the physician's office to a lab. Given the nature of this test, white blood cells must be frozen and separated, which cannot be done by a doctor. The samples have to be transported frozen and in batches given the logistical costs. As such, Life Length began building partnerships with major diagnostic labs worldwide, many of whom contacted us, and we now have 13 such partnerships. This model is proving to be successful, as we can also take advantage of these labs' commercial infrastructure to sell our TAT to physicians.

We believe that the TAT test has the potential to become a biomarker on par with cholesterol testing, which is the largest biomarker in the world today by sample volume and revenue. Our vision is that Life Length's test will become over a period of time an increasingly standard part of preventive healthcare as well as a test used by cardiologists, oncologists, infertility doctors and endocrinologists, among others, because of its correlation to all these diseases. This means we must also make this test more affordable, but that will inevitable happen as we scale the technology.

How do you plan to expand the company further, and do you have an exit strategy?

We currently bring all samples worldwide to our lab facilities in Madrid. During 2015, we intend set up a lab in the US, our biggest market, and in the next few years we believe that it may be possible to establish about five labs in strategic locations around the world, such as in Southeast Asia, Japan, China and India. We will continue to use our lab in Madrid as the R&D hub to improve our technology and to process European samples here, while other facilities will function as production

labs to deliver results to clients.

We are in the early days of telomere biology and there is huge potential for not only improving the technology but also extensively broadening its application. In terms of an exit, many things could happen and this is in the future. If we succeed in implementing our vision of converting our TAT in to a standard biomarker and the market indicates that this potential exists, just one percent of the testing volume of cholesterol in ten years would imply around eight million tests. Hypothetically if the test cost $50, that could generate $400 million in sales. At some point, Life Length could have two ways to create liquidity for its investors: either through an IPO, or more likely the company would fit in as an acquisition for a pharma or diagnostic company with a much bigger commercial infrastructure.

What can other companies in Spain learn from the success of Life Length?

We have put together a business plan and team that is not just about science but also delivering a commercial service, the latter of which helps generate revenue. Raising capital is very hard for early stage companies, and Spain is not a traditional bastion for this kind of business. Giving visibility that this is a service which customers want to purchase is the best way to give comfort to potential investors and to be able to raise capital for your business. Life Length has succeeded in raising capital because we are generating revenue, and we are generating revenue because we have built a business around a very good technology that would not generate sales by itself. Understanding what the market needs and delivering a service is fundamental to building a successful company. Get to the market as soon as you can, execute on your business plan and demonstrate that the market wants to pay for your service.

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