Saad Harti – President, Legacy Healthcare, Switzerland



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05.10.2017

Tags: Switzerland, Legacy Healthcare, Botanics, Pharma, Chronic Disease, R&D

Saad Harti, president of Legacy Healthcare, discusses the company's origins, their unique focus on side-effect free botanical drugs for chronic conditions, and the importance of stakeholder education in this exciting but still immature field.

What was the initial inspiration for setting up Legacy Healthcare back in 2007? How did you come to choose to found a business dedicated to developing side-effect free botanical drugs for chronic conditions?

Legacy Healthcare is actually the second life sciences company that I have founded. My first venture was a licensing and distribution business called AltaCare, which I established in the early 2000s and it was actually partly the experience and proceeds from this entity that were harnessed to initiate Legacy. The inspiration to get involved in the botanical drug segment derived from my realization of some of the shortcomings of the synthetic drug industry relating to treatment of chronic conditions and my gradual understanding that current treatment pathways, in many cases, no longer fit with what patients truly expect from a treatment for their chronic disorders: improve quality of life, without triggering other issues, due to unknown long-term toxicity.

What made you come to the conclusion that synthetic drugs are not fit for purpose for many chronic conditions?

Today, the vast majority of medicines that we ingest tend to be chemically synthesized, potent compounds with unique mechanisms of action, but side effects ranging from mild to deadly, and generally unknown long-term toxicities and unpredictable drug-drug interaction. This treatment methodology, however, is far from desirable in a world in which fewer people are dying from acute illnesses, but more patients find themselves needing to live with and manage prolonged chronic disorders, generally non-life threatening, but still, requiring treatment. While contemporary patients are willing to accept adverse side effects when life is imperiled such as when they are afflicted with instances of aggressive cancer or infectious disease, they are far less ready to tolerate them when it is not a matter of life and death. In short, the market is demanding better, more patient-centric medicines where quality of living is not so easily degraded.

Meanwhile incidence of severe side effects from classic medicine is becoming a real health risk of itself. The FDA, for example, estimates that adverse drug reaction has become the fourth biggest cause of mortality in the United States and that a full 42 percent of American citizens over the age of 65 are taking on a regular basis a concoction of five drugs or more. The cost of adverse drug reactions mortality and morbidity was estimated to be USD 177 billion in 2004. And during the 2004-2014 period, side effects reported to FDA increased five-fold. That gives an idea of what these costs might be now. Not all botanicals are safe, but by using extracts from the one our bodies are used to ingest, we have all chances to develop very safe drugs, with little side effects and long-term toxicity. By betting big on botanical drugs, we are hoping to contribute to the breaking of this vicious cycle. We believe that Legacy Healthcare can contribute in developing much more patient-friendly drugs that can serve as a useful complement to classic, synthetic medicines.

Are patients, physicians, healthcare providers and drug developers sufficiently aware of the extent of this phenomenon?

Well you could call it a silent pandemic because the full extent of the side effects derived from the repeated taking of many classic drugs over a prolonged period of time to treat the symptoms of chronic disease is still rather poorly understood. Though new compounds entering the market have to pass rigorous evaluation process to ensure that they are fit for human use, the majority of the products that will secure authorization have been tested for only one year at best. No one can be completely sure of what the the extent of side effects, long-term toxicities and drug-drug interactions will be if a patient repeatedly takes that product over the course of a decade. It may be that many of these drugs are ticking time bombs in the patients’ bodies, especially when

combined with a concoction of other potent compounds and in a restricted population (age, ethnicity and sometimes gender).

From time to time, a toxicity-related health scandal blows-up. The industry seems to consider them as necessary evils. But their frequency is increasing; patients are becoming more vocal and information is available to everyone now.

That said, patients themselves, are becoming much more discerning when it comes to following physicians' prescriptions. The last decades have witnessed a real empowerment of patients who now have much more access to information and are willing to challenge the advice of their doctors. As I mentioned earlier, patients' behavior and preferences are evolving and we are seeing a surge in demand for patient-centric treatment pathways that offer a better quality of life. Last September, I attended FDA's Public Meeting on Patient-Focused Drug Development for Alopecia Areata. The purpose was to hear patients' voice in order to set the endpoints FDA will start asking for from drug development companies. Side effect and long-term toxicity were as important as efficacy.

The industry seems much slower to adapt. In just the same way as customer (and regulatory) demand is forcing the car industry to be more environmentally friendly and pushing for the substitution of petrol power with electricity, the drug development industry will be forced to adapt their offering. As is often the case, the consumer leads the way and the industry follows, albeit with some reluctance.

I do believe, though, that payers and healthcare providers are beginning to acknowledge the need to shift the paradigm and come up with treatment solutions that carry fewer adverse side effects, though not comprising efficacy. The US authorities have recently calculated, for example, that dealing with adverse drug reaction is costing more than the expenditure required to treat diabetes or cardiovascular disease. This means that treating chronic illness patients in this manner is not only producing very negative health outcomes, but also potentially jeopardizing the financial viability and sustainability of public healthcare systems. Not surprisingly payers and policy makers alike are becoming increasingly keen to incentivize and facilitate alternative solutions.

How do your botanical products represent a viable alternative solution?

At Legacy Healthcare, we take botanical ingredients that people consume on a regular basis and turn them into drugs. Our drugs have fewer, and considerably less severe side effects, if any, than

synthetic drugs. They inherently register much better tolerance profiles because rather than extracting a single molecule, we take everything so what is being consumed is as close as possible to what people would be ingesting naturally on a regular basis. Incidentally this also means that we can collect data from the public domain, which you obviously cannot do with a brand new, untested chemical entity, so there is even an acknowledgement of a priori safety. To avoid raised eyebrows from our peers, I can confirm that botanical drugs can be patented.

Once they have secured the appropriate authorizations, then these drugs can be prescribed, used, reimbursed as any other drug.

Most of our current emphasis is on alleviating side effects of cancer treatments, also called oncology supportive care. If you think about it, cancer can increasingly be regarded as a chronic illness because many people are today surviving cancer, but ending up with a substantially reduced quality of life following the affliction. Because cancer hits you everywhere, synthetic chemical medicines with onerous side effects often have to be deployed to counter the disease. It makes little sense, however, to be prescribing additional drugs carrying yet more side effects. Far better, wherever possible, to instead utilise reaction-free botanicals drugs at this particular stage when the patient is already highly medicated. Our CG428 candidate is a great example to illustrate this point: this is a highly effective botanical hair lotion geared towards helping re-establish the natural balance of the hair cycle when disturbed by chemotherapy and hormonal cancer treatments. In Japan for instance, oncologists use it on a compassionate basis already, while the development process is on-going.

Do you not face a certain amount of industry skepticism when trying to place botanical products on the market? How accepting are people of the efficacy of these sorts of remedies?

The first product we have developed has been commercialized by Sanofi, Abbott and Galderma-Nestlé Skin Health, all pharmaceutical firms. Provided the science is solid and the proof of efficacy and safety are there, the industry understands the benefit.

The skepticism comes from the Venture Capital funds, which we need, as a drug development company. Therefore, we do encounter an element of skepticism from some quarters because this is a new segment of industry that is still trying to make a name for itself. To date, the FDA and EMA have approved only three innovative botanical drugs in total so there is a lot of work to do in order to get this niche, with huge potential, flourishing. Legacy Healthcare sees itself very much as one

of the first movers and pioneers.

It is important to understand that, when we take a botanical drug through the FDA or EMA process, we are delivering the exact same pathway and clinical package as for synthetic compounds. The rigor of testing, the expense and the trial design are almost identical. Admittedly the size of the trial may not be as big, and therefore less capital intensive, but that is completely logical because these substances have an a priori level of usage and a larger quantity of data to back them up.

How can you surmount this obstacle?

I believe that it is only a matter of time before a tipping point is reached. Consumers are already starting to demand safer types of therapy with fewer side effects and regulators are fast becoming conscious of the drawbacks of sustained overconsumption of many types of synthetic medicine. It won't be long before the pharma industry starts to react to these pressures and the venture capitalists and rest of the investor community will rapidly follow suit. Even in the short space of time that we have been operational we have found the healthcare authorities to be increasingly supportive.

Moreover, it should not be forgotten that pharmaceutical firms themselves have been backing our products, as well as prestigious research institutions.

How do botanical drugs fare in terms of patent protection?

Interestingly, botanical products enjoy a certain amount of insulation from being copied because of the challenges in manufacturing and standardization. Whereas single molecule generics are easy to produce, botanicals are rather more complex because the end product will be affected by how you harvest and process the raw ingredients. One of the major challenges in botanical drug development relates to how you ensure that each batch being used in a trial is the same and is exhibiting the same degree if properties. We, at Legacy, have been hard at work for 5 years to overcome these sorts of obstacles. The up-side to this is that the day our patents and patent extensions come off, it will be difficult for new entrants to make the perfect bioequivalent copy without access to additional trade secrets. This should be of great interest to both potential scientific partners and also the investor community. The barriers to entry surrounding the botanical drug development industry are such that we are unlikely to see quite the same dynamic as the patent cliff that is so common with classic pharmaceuticals.

Another advantage botanical drugs may bring is in drug pricing and drug access. Drug development has become very costly, with the consequence that drugs need to be priced at levels never seen before to enable return on investment. In the countries which can still afford reimbursing them, this is creating financial pressure. And in the countries who can't, these drugs will not be available for years; increasing the gap between the haves and the have-nots. Long story short, because they are safer, the development cost of botanical drugs is less than for synthetic drugs, enabling the setting of lower prices, while still being profitable.

With lower prices, botanical drugs can also be affordable to people who are not covered by insurance – so almost everyone outside the western world – from the moment they become available. From a pure business standpoint, we increase our patient base, which is great. Bottom-line, it's a win-win-win-win situation. Win for low-income countries, win for the payers in rich countries, win because the costs of adverse events will be much, much less, and win for the drug companies. It is a change in paradigm.

What are the next steps for Legacy Healthcare looking forwards?

This is a very exciting time for the company. Our most advanced program in pediatric alopecia areata has been authorized by EMA to enter phase III. We are the most advanced program out there for this type of condition and, if all goes well, we should be able to have a treatment on the market by 2021. Patients and parents are increasingly concerned about the side-effects of drugs being given to their kids for this type of autoimmune disease that will require ongoing management, so there is massive demand for a product like ours that displays a superior safety and tolerance profile. Now we have to confirm its efficacy.

Our second most advanced product is for chemotherapy induced hair loss and Swissmedic has authorized us to enter phase II, which has started, while we also have a trial ongoing in Japan. A major priority will also be to build partnerships and secure new sources of funding so as to be able to accelerate our rate of development. The expertise that we are amassing on how to develop botanical drugs will serve as a base for our future endeavors. The ambition is to become a powerhouse, pioneer and champion of this exciting new industry.

Remember that most people would not bet a dime on Tesla a decade ago; now the whole car industry is shifting to cleaner cars.

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