Fernand Labrie – President and CEO, Endoceutics

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Dr. Fernand Labrie shares the significant achievements of Endoceutics, in launching its first breakthrough product for post-menopausal vulvar and vaginal atrophy, known as the 'female Viagra', the innovations behind the specialty area of 'intracrinology' that he discovered, and his perspective on the importance of homegrown innovation for Canada's development.

Having met with you four years ago, what have been some of the major changes for Endoceutics since?

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A main goal in 2013 was to build a truly complete Canadian pharmaceutical company with operations along the entire value chain of drug development. Today, we have our in-house R&D in Quebec clinical research organization driven from Quebec, manufacturing in this facility here in Montréal, as well as our first product on the market in the US, so I am proud to say that we have accomplished this.

Intrarosa® is our flagship product and in November 2016, it was approved for the treatment of moderate-to-severe dyspareunia (pain during intercourse). This is a common symptom of post-menopausal vulvar and vaginal atrophy (VVA). As it is a vaginal insert not manufactured anywhere else in the world, we also acquired this facility in Mont-St-Hilaire in January 2017 for its manufacturing capacity, in addition to sourcing materials from Mexico and the US.

In line with these developments, we decided to rebrand Endoceutics with a new and more modernized logo this year. The previous logo had been in place since Endoceutics was founded in 2006 and it was time for an update!

Can you tell us more about the exciting innovation behind Intrarosa®?

Fundamentally, we take a non-estrogenic approach to the development of these novel treatments, using a precursor compound inactive by itself, dehydroepiandrosterone (DHEA), which is a very important but previously unrecognized source of all sex steroids in women after menopause.

To provide some context, earlier in my career, I had discovered and developed medical castration with GnRH agonists as well as combined androgen blockage – this was the first treatment shown to prolong life in prostate cancer, and 30 years later, this is still the only treatment. It is the standard hormonal therapy for prostate cancer worldwide, and the basis behind the success of recent new blockers of androgen action from Big Pharma like Astellas and AstraZeneca.

In prostate cancer, we realized that when we removed the testicles from men with that cancer, testosterone levels in the blood decreased by 97 percent. But in the prostate, the levels only decrease by 50 percent, which means androgens are coming from elsewhere – and this is how we discovered DHEA (prasterone), a compound inactive in itself but the precursor of estrogens and androgens. In prostate cancer, you block this mechanism because you do not want to stimulate the cancer.

For menopausal women, it is the opposite. Serum DHEA levels decrease by 60 percent on average before menopause, which is why women face sexual problems like low arousal, low desire and low orgasm rates. After menopause, when estradiol production by the ovaries stops, DHEA continues to be secreted (at decreasing concentrations) by the adrenal glands and is distributed to all tissues, where it is transformed locally. Natural levels of DHEA vary between women.

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The breakthrough was really discovering that local application – applying the drug vaginally – worked. Everyone had thought that sexual arousal was a problem in the brain, but this is not true. The brain does not decide physical responses on its own; it depends on external stimuli as well, so our product introduces androgens directly to nerves within the vagina in order to stimulate them. No one had ever developed this product before – and in fact, its benefit is that with local application, with the right dosage, the maximal effect can be achieved without having hormones entering the blood, to avoid any association with breast cancer rates.

However, with this intracrine mechanism, without any side effect, each tissue makes what it needs, in the right amount, and it is degraded locally. It does not leak into the blood. For this reason, FDA approved Intrarosa® without a black box – the first and probably only drug ever to receive approval without any side effect! This is because we are replacing what the body is naturally missing, in a small amount, locally.

How significant is the unmet medical need in this field?

Intracrinology is a newly established field within women's health. There is definitely a huge and pressing unmet medical need here. To give an indication, in the US, 32 million women suffer from vaginal atrophy symptoms like dryness and pain during sexual activity. Yet only one million currently receive treatment – less than 3 percent.

More generally, menopause is a condition that will affect every woman as she ages. In 1900, life expectancy was 47 years. Today, it is 82. As medical advancement extends life expectancies, invariably, the prevalence of age-related conditions will increase as well.

Estrogen-based hormone replacement therapy (HRT) was the only form of treatment. However, recent findings have indicated that estrogen supplements increase the risk of breast cancer, which is a very serious condition for women. It is difficult to treat because it spreads into peripheral tissue very quickly, and once it is detected, it is very frequently too late to treat it. There was no well accepted treatment available. Furthermore, many women tend to accept these symptoms as a natural and inevitable part of aging. The prevailing attitude was simply, 'we have to live with this'. As a result, sufferers and doctors did not discuss these issues. A lot of medical education still needs to be done in this area.

Given all these considerations, what will be your commercialization strategy for Intrarosa® in the US and globally?

Intrarosa® was approved by the US FDA in November 2016, and we have out-licensed the product to AMAG Pharmaceuticals. We are currently working on a commercial plan for the launch. I believe the direct-to-consumer approach is very important; there are perhaps 330,000 health professionals we need to reach, as well as nurse practitioners and general practitioners.

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We expect to receive approval from Health Canada by the end of the year, and we have also begun the market approval process for Europe. The ultimate goal is to launch Intrarosa® across the world, including markets like China and Japan. We hold patents until 2031 in the US and around 2028 in the rest of the world which puts us in excellent position moving forward.

What else does Endoceutics have in its pipeline?

The most exciting one is a combination therapy currently in Phase III clinical studies, which combines DHEA with acolbifene for the treatment of vasomotor symptoms, prevention of breast cancer, and osteoporosis.

We have four other Phase III product candidates as well as two in earlier stages. We hold exclusive global rights to patents, patent applications, technology and know-how related to all our products.

Having applied for market approval in Canada, how do you assess the current market access landscape locally?

We had concentrated on the US as our first launch country so I am not very familiar with the Canadian market access environment. Nevertheless, I understand that product reimbursement is rather difficult in Canada, and we are in a period of reforms where regulatory agencies and the governments are basically looking at decreasing drug prices – much like their counterparts in Europe.

I think an equilibrium needs to be struck between drug prices and an attractive market in order to support R&D, for both new and innovative drugs, as well as homegrown R&D and innovation. There are countries with lower drug prices than Canada but it is difficult for industry to launch new products in these markets, which means less choice for patients and healthcare practitioners. Similarly, if Canada wants to attract R&D in the domestic healthcare and life sciences sector, there needs to be a commercial incentive for industry.

How do you evaluate the Canadian R&D and innovation ecosystem?

The quality of Canadian R&D and science, from basic to applied and clinical, is excellent, but there is insufficient support.

A few years ago, I had the pleasure to meet our former Prime Minister, Paul Martin. I had made calculations on the difference between Canadian and American per capita spending on medical research: it was a fivefold difference in favor of …. the US. He was stunned and said he had never heard about that before. In the next Budget, the Federal government subsequently increased the budget for medical research. This has, unfortunately, never happened again since.

The success rate of medical research hovers at 15 percent or so, which is tiny and discouraging for researchers.

This is where there needs to be much more funding, as well as funding sources, across Canada. Currently, there is only one federal funding agency, the Canadian Institutes of Health Research (CIHR), so if researchers miss out on that, they are out of options. This is in stark contrast to the funding landscape in the US.

As an indication, the total cost of bringing Intrarosa® to market is CAD 265 million. I funded this personally through the royalties from my previous work in prostate cancer. Medical and health research is extremely expensive. The current clinical trial we are conducting will cost us around CAD 25 to CAD 30 million!

How rich a country is – truly – depends on innovation. Talking is not enough, there needs to be action. We rely too much on natural resources. When you buy an iPhone at CAD 1,500, that is the product of innovation, not natural resources. I think the Canadian government needs to invest significantly more across the entire research value chain.

Given its proximity to the US, the largest pharma as well as innovation market in the world, what role can Canada really play when it comes to fostering local innovation?

It is not competing with the US, it is about bringing our share of innovation to fruition in the world. We did it ourselves with Intrarosa®, which shows that Canada definitely has the potential for such successes.

In today's globalized world, borders do not really represent limits on innovation.

What vision do you have for Endoceutics?

I would like to establish Endoceutics as a global leader in women's health. I actually have some ideas in the area of men's health as well, but – let us take care of the women first!

Do you have any advice for aspiring pharma entrepreneurs looking to establish their own 'complete' company?

The giants have become too big – there is constant M&A activity within the industry. I would recommend them to build their own companies. If you do it yourself, you have control over the process and company activities. Otherwise, you have no control.

Anyone that has a good idea should not hesitate. They should work hard for it. Being smart is not good enough; you have to understand the basics, but you need to work hard, very hard, more than average. Life is short, so you should not waste time: choose the right things to pursue, and work hard!