FrÃ©dÃ©ric Cren â?? Chairman, CEO & Co-Founder, Inventiva, France

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Inventiva is a French clinical-stage biotech company focused on developing oral small molecule epigenetic modulators in therapeutic areas with high unmet medical needs such as fibrosis, lysosomal storage disorders and oncology. Its most advanced program is a first-in-class drug candidate against NASH. Inventivaâ??s chairman, CEO and co-founder, FrÃ©dÃ©ric Cren, explains how the company leverages its unique assets to deliver its R&D strategy. He also outlines the successful partnerships the company has struck with Big Pharma. Finally, he emphasizes the attractiveness of France as a hotspot for science, innovation and entrepreneurship in the life sciences industry.

Prior to co-founding Inventiva, you had an extensive career in Big Pharma, first with Fournier Pharma acquired by Solvay, itself acquired by Abbott where you occupied the position of General Manager of research. What was the motivation behind starting your entrepreneurial journey?

We were presented with the opportunity to acquire several valuable assets from Abbott that we considered to have the potential to be one of the best in the field. These assets originally came from Fournier which had developed a strong know-how in nuclear receptors and targeted epigenetic modulation of gene expression that continued to be developed by Solvay and Abbott. In addition to these assets, Inventiva acquired Abbottâ??s state-of-the-art R&D infrastructure which came with a talented and experienced team. As a result, we had all the right ingredients to build a successful company.

Our focus is on developing oral small molecule epigenetic modulators. We have an extensive library of approximately 240,000 pharmacologically relevant molecules, 60 percent of which are proprietary, as well as a whollyâ??owned R&D facility, which can help us generate new chemical matters. Our expertise has been recognized by big pharma players as we have established two promising partnerships with AbbVie and Boehringer Ingelheim, which reinforce our credibility towards investors and other large pharmaceutical companies.

Your most promising drug candidate called lanifibranor is being investigated as a potential treatment against non-alcoholic steatohepatitis (NASH). Why did you decide to pursue this indication?

We are focusing on NASH with lanifibranor since the mechanism of action of this pan-PPAR agonist is well-established for this indication: it has the potential to reduce lobular inflammation, hepatocyte ballooning and fibrosis. It also improves insulin sensitivity which is a distinctive feature compared to other competitive programs and really important given that nearly one NASH patient out of two also suffers from diabetes. We are currently conducting a large global Phase IIB trial in more than 90 sites around the world, including in the US, Europe, Australia and Canada. The trial progresses as planned and we expect results in the first half of 2020.

Another promising asset is odiparcil, a drug candidate that you are developing for the treatment of mucopolysaccharidosis (MPS), a group of rare, progressive genetic disorders. Odiparcil has recently received â??Rare Pediatric Disease Designationâ?• by the U.S. Food and Drug Administration for the treatment of MPS type VI. What does this mean for the future development and commercialization of the molecule?

Odiparcil is an incredibly interesting program in a therapeutic area with high unmet medical needs. Patients are currently being treated with enzyme replacement therapy (ERT) that leaves them with a huge medical gap. If you look at the needs of MPS patients, it does not take long to realize that another approach is needed. The first advantage of odiparcil is that it is an orally-available small molecule, which is greatly preferable to weekly ERT infusions at the hospital. Moreover, odiparcil has shown very promising results as a stand-alone treatment in relevant preclinical models. Its clinical development is progressing well: we are currently running a clinical Phase IIA trial for the treatment of MPS type VI with results expected in the second half of 2019. Odiparcil has already been granted both orphan drug status and Rare Pediatric Disease Designation by the FDA for the treatment of this indication. This means that the resources needed to develop and bring the drug to market will be substantially less than for other programs such as the one for NASH. Moreover, in the case of MPS, regulatory agencies tend to be more open to discussion as they realize the patient population is small, the disease is extremely severe, and the unmet medical needs are high. Patient associations are also very welcoming of innovative therapies such as odiparcil. Finally, receiving Rare Pediatric Disease Designation also means that once the product is approved, we will be eligible to receive a Priority Review Voucher by the FDA which can be either redeemed to obtain a priority review for a future submission of a new drug application or sold to a third party. The last voucher sold a couple of days ago for about EUR 100 million.

More recently, Inventiva started research to discover a new cancer drug. What are your ambitions in this therapeutic area?

Our YAP-TEAD program targets a novel pathway, the so-called Hippo signalling pathway, which plays a key role in the oncogenic process, for the treatment of non-small cell lung cancer and mesothelioma. With this approach, we believe we are leading the field in this area. YAP-TEAD has shown very promising results in vivo in monotherapy but also in combination with approved cancer therapies. We have especially demonstrated our compoundsâ?? potential to significantly reduce tumor growth, attenuate multidrug resistance and re-sensitize chemo-resistant cancer cells. Until now, we have mostly developed in vivo and in vitro models internally. In addition, we have established a strong collaboration with some of the most knowledgeable groups in the field of oncology of the Institut Curie. We also collaborate with the Institut Gustave Roussy, one of the largest oncology centres in Europe, to help us design the Phase I/II clinical trial. We are currently in the process of selecting a clinical drug candidate for our YAP-TEAD program, which we anticipate entering pre-clinical development later this year.

In recent years, France has been losing attractiveness as a clinical trial destination. How would you assess the attractiveness of France in the space?

Conducting clinical trials is always a difficult process no matter the country. Moreover, all countries have their specificities. For instance, at Inventiva, we have faced more challenges in Spain and Italy than in France. Is France better or worse than other countries? The answer is not that clear-cut. What I can say is there are very experienced and state-of-the-art clinical centres in France. However, there are some regulatory challenges that lengthen market access timelines. Last year, a welcomed reform was introduced to make clinical set-up easier, but more needs to be done.

What is the scope of your partnerships with AbbVie and Boehringer Ingelheim?

We started our collaboration with AbbVie in 2012 from scratch. The idea was to develop an orally-available ROR gamma agonist for the treatment of several rheumatic autoimmune diseases. The program was very successful so far as we were able to develop a drug candidate, ABBV-157, for the treatment of moderate to severe psoriasis that entered Phase I. The clinical development is now the responsibility of AbbVie. Since 2016, we are repeating the same model with Boehringer Ingelheim in the field of idiopathic pulmonary fibrosis.

Both collaborations entitle us to receive milestone payments upon the achievement of pre-clinical, clinical, regulatory and commercial milestones, in addition to royalties on any approved products resulting from the partnerships.

Through these collaborations, our scientists have learned how to work with Big Pharma and we have all the required infrastructure to manage and transfer relevant data efficiently and securely.

What other opportunities for partnerships do you see in the future?

Our patients, competitors and partners are everywhere in the world, so we view ourselves as a global company. Although our origins are French, we have an international team with deep expertise in the fields of biology, medicinal and computational chemistry, pharmacokinetics and pharmacology.

Regarding partnerships, it really depends on the molecule. Some assets are more adapted to be developed internally, while others require a partner either because they target large populations, competition is fiercer or because we simply do not have the expertise.

One of the major challenges for biotech ventures is access to funding. While Inventiva is listed on Euronext, the majority of the shares are owned by the founders. How do you go about raising funds for the company?

Fundraising takes up a large amount of my time. In France, access to seed money for the start-up phase from public and private actors is relatively easy, but scaling-up is harder. We need to look beyond French borders and have been actively looking for investors in the US as this is where the relevant institutional investors are. During the last private round of funding in April 2018, half of the EUR 35.5 million gross proceeds came from the US and half of the participants were new investors.

What strategic objectives would you like to achieve in the next five years?

By the end of this year, we will be able to present Phase IIA clinical results for odiparcil (MPS type VI) and to select a drug candidate for our YAP-TEAD program in oncology. During the first half of next year, we will present Phase IIB clinical results for lanifibranor (NASH). Beyond this point and if results are positive, our strategy will be very different for the two candidates. As NASH is a very large indication, we will be looking to partner with a Big Pharma company. For odiparcil, we plan to continue development and marketing on our own. Finally, we need to keep innovating with new R&D programs. This is what we are good at and we should continue doing it.

Do you have a final message for our audience?

I think the science and entrepreneurial environment in France is excellent. We have great scientists and a strong network of entrepreneurs. Developing a pharmaceutical compound is not something you can learn overnight. France has been at the forefront of drug development since the beginning. Because of these reasons, I believe French biotech companies have what it takes to reach success. We will deliver results; it is only a matter of time!

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