

Declaration from the Josep Carreras International Foundation regarding its participation in translational research spin-off companies created by the Josep Carreras Leukaemia Research Institute

- To be able to pass on scientific advances from the scope of basic research, where they originate, to their clinical bedside application, large economic resources are needed that neither the Foundation, the academic world nor the public sector can provide. Concentrating the available resources on a few lines of research, which may progress or be invalidated once their industrial and regulatory development begins and experiments are done on humans, would make it impossible to progress in others.
- This area of development and transfer of knowledge is known as “translational research”. Its objective is to validate the basic research, in a mechanistic manner and often focused on animal models, for use in humans, so that the advances can reach the professionals and patients. To do this, companies are needed that can deal with the regulatory implementation (industrial scaling of the manufacturing; toxicology and safety tests prior to administration in humans; clinical trials; and global distribution capacity). At the moment, western health systems do not have the mechanisms to make cutting-edge science accessible to patients in a generalised or universal way. Neither the academic sector nor the public sector can finance these stages and, for this reason, spin-off or spin-out companies are created, which are, in reality, instruments that transform biomedical knowledge of academic origin into therapeutic products and services of generalised application, principally financed by private investors.
- All spin-off type companies have a very important instrumental component. It is worth stating that the term *spin-off* has legal connotations and is regulated by the current Science Act. It defines those companies created from academic research in which the institutions that generate the technology participate in the shareholding. Having the status of a *spin-off* exempts researchers from certain restrictions imposed by the Public Administrations Act, so they can reconcile their research and teaching work in the public sector with business administration, management, and research in the spin-offs.
- There are specialist investors in the field of life sciences who use their funds, in an explicit and strictly regulated manner, to invest in newly created spin-offs to allow development of new therapeutic options; being fully aware that the rate of success is low. Therefore, we start from the premise that the academic discoveries, which are mainly mechanistic, can only reach patients in a robust and permanent manner if the risks of the investments and the future are assumed by private capital in a corporate instrument. In these projects, profit is secondary to the primary objective, which is to **solve a medical problem**. If it is solved, it generates profits, but the TECHNICAL probability of success is extremely low (less than 1%). Normally, the translation of knowledge is analysed in the opposite way to a normal business; instead of seeing whether there is business in an unmet area of the market, they see whether there is an unmet medical area and which business must be implemented to solve it. The driving force is always how to solve a medical problem. The business plan is designed to obtain the necessary capital to solve it. And the specialist investors invest in these companies with the premise that a small percentage of their partners will end up validating the founding hypothesis and generating earnings. Even so, no specialist investor will invest in a newly created spin-off unless the founding science generates sufficient expectations regarding the solution of an unsolved medical problem, and without visualising a possible commercial outlet (normally a transaction with a global pharmaceutical company) that generates a large return on the initial investment.

- In this sense, thanks to the good work of its researchers, the Institute is in a position to licence its own patents to companies that undertake to finance the translational stages and arouse the interest of the aforementioned investors. The Institute can create these companies together with other agents involved in the basic research, such as the ICREA Foundation and the researchers, who often, by working in teams with researchers from other institutions, generate intellectual property with multiple co-owners. These also end up reflected in the shareholding stake of the spin-offs, should these end up being the best option to implement the technology for patients.
- It is normal for the financial investors to ask the founding scientists and promoters of spin-offs to accompany the former's investment within the scope of their possibilities. This is a very important aspect as it visualises the concept of "shared risk" of these projects and confers great trust. Being the main promotor of the research activities of the Institute, **the Josep Carreras Foundation** incorporates a very important additional component, the **reputation component**. For any observer, financier or otherwise, the fact that the Foundation accompanies an investment associated with the creation of a spin-off of the Institute represents a direct endorsement of the project and its objectives, which transcends the economic aspect of an investment in the classic commercial sense of the word.
- This is very important from the perspective of future financiers (private investors, public entities, the EU, companies that want to become possible industrial partners). Bear in mind that the initial rounds of capital are only the first stage, and that each subsequent stage entails a change in scale of the financial needs. In other words, the **Foundation's initial support, accompanying with capital, within its possibilities, the Institute, the investors and founding scientists, is extremely important not only for the initial investors, but also for those that will come later** (including institutional investors), which will be quite a few. In the recent case of OneChain Immunotherapeutics, for example, this involvement, apart from facilitating the final decision of the lead investor of the round, also allowed for the CDTI of the Ministry of Industry, through its co-investor instrument Innvierte, to commit to almost double the contribution made by the Foundation, as, from what we find, the Foundation's endorsement provides an added degree of gravitas and trust.
- The Foundation's contribution may be materialised in many ways: as a non-recoverable investment through the Josep Carreras Leukaemia Research Institute, or by participating directly in the spin-offs created by the public research sector. When there is the possibility of creating a spin-off, **the Foundation's contribution has a clear mobilizing and multiplying component**, a very evident anchoring effect, as we have been able to verify. Also, as spin-offs normally maintain a close relationship with the parent institutions (renting spaces or subcontracting research projects or services, including researchers), the Foundation's contribution in terms of capital ends up returning in full to the Institute in the short term.
- On the other hand, **the Foundation's direct participation in the shareholding of the companies gives it significant powers to control the rigour, ethics, and evolution of the spin-off**. The Foundation's objective is not to obtain financial returns but to **guarantee the founding purpose of making scientific advances reach the highest number of patients as quickly and safely as possible**, and to prevent this objective being contaminated by other material considerations. In this way, the Foundation's shareholding protects the transferred technology, guaranteeing that it is developed with the greatest diligence for the initial objectives of the spin-off. And in the event that the technology reaches the patients and is distributed globally, solving an unmet medical problem, it will be associated with a **significant economic return that, in reality, is no more than a collateral effect of the project's success, but is not the reason why the Foundation invests**.

- The Foundation's statutory mission literally states: *"To achieve the founding aims, the Foundation carries out the activities that the Board of Trustees deems necessary directly and/or in collaboration with other entities, institutions or people, public or private, with the widest scope, in accordance with the provisions of the legislation regarding foundations."* So, the premise is that, to make the most suitable instrument to reach the patient, a spin-off may often be necessary, and that, to make this company feasible in the long term, the Foundation's capital contribution has a very clear multiplying anchoring effect (particularly in projects with a lot of technical and commercial risk, associated with rare or paediatric diseases or those without clear therapeutic alternatives; projects in which it is extremely difficult to attract private investment). This contribution also returns indirectly to the Institute in the short term and allows greater control over the business management of the transferred technology.
- Based on these reasons, for transparency and public knowledge purposes, the Josep Carreras International Foundation declares the following:
 - o The participation of the Josep Carreras International Foundation in the shareholding of spin-off companies in the field of translational research aims to ensure scientific rigor and guarantee the fulfillment of the founding aim of scientific advances reaching all patients quickly and ethically.
 - o The Foundation accompanies the initial investment of the company creators and that of other investors who join in later stages as a sign of support of the transferred research and the founding team, taking into account that the projects are targeted to minority, low-prevalence, pediatric hematologic tumors or those with few therapeutic alternatives.
 - o The Foundation undertakes to reinvest all the dividends, reintegrated capital and capital gains that its participation in spin-off companies generates primarily to the research projects of the Josep Carreras Leukaemia Research Institute, a fully public center of the CERCA network. of the Generalitat de Catalunya.

Thank you.
Antoni Garcia Prat
Management – Fundació Josep Carreras