PHARMACEUTIQUES
Drug, Health and Industry

HEALTHTECH INVESTOR DAYS:
SPECIAL ISSUE

DEFINING AND PROMOTING NEW PATTERNS OF INVESTMENTS IN HEALTHCARE

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HTID special edition

European HealthTech
A Question of Health... and Sovereignty


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Hervé Réquillart
Editorial coordinator

For some years now, experts have been warning about the funding of health-care start-ups. The situation is well known. The European ecosystem has all the tools it needs to bring innovation through to the business start-up phase. Beyond this point, however, it offers scant tools to companies once their financial needs exceed the €15-million mark. Meanwhile, on the other side of the Atlantic, but in China too, innovative companies are "covered" by large funds, which "risk" amounts sometimes in excess of $100 million and take care to accompany the firms involved through to maturity and often beyond. It is in the face of these observations that the first HealthTech Investor Days (HTID) were set up. By bringing all the players in the sector – investors, start-up executives and big pharma companies, scientists and institutions – together around the same table, France Biotech intends to participate in the consolidation of Europe healthcare innovation that is still fragile, seeking to attract funds from any source, whether European, American or Asian. Only a powerful syndicated investor movement can give start-ups the ability to develop their innovations at home in Europe and to respond without delay to manifold patient needs. The challenge is, of course, medical and clearly economic, but it is also deeply political. Innovation in health is after all a central factor in the sovereignty and independence of the European continent as a whole.

Coming of Age of the European Ecosystem

As was already apparent in the early stages, the European HealthTech ecosystem is now being driven forward by major public and private initiatives. The European Institute of Innovation and Technology (EIT), EuropaBio and the European Investment Bank are among the driving forces behind this new attractiveness.

The European HealthTech sector is young. According to Pierre Courteille, Chief Commercial Officer and Vice President Business Development at ABIVAX, it is indeed twenty years behind! "In the United States, it emerged in the 1980s in Boston. At home, however, it only took off in the 2000s." The United States, the world's largest healthcare market, is now more than ever attracting investors from around the world. However, no one denies the potential of the European market. All the experts agree upon the high quality of its fundamental research, universities and technology hubs. These strong points are now supported by national authorities.

Attractive Fiscal Policy

One of the key areas of a country's attractiveness today is taxation. In the United States, the reform under Donald Trump's administration, approved at the end of 2017, has thus encouraged the repatriation of profits made abroad by American companies. These represent lost investments for European companies. However, innovative companies in Europe also benefit from tax incentives. In France, for example, the research tax credit enables SMEs to deduct 20% of their innovation spending. According to a study conducted by the French National Commission for the Evaluation of Innovation Policies (CNEPI), the expansion of the scheme in 2008 resulted in a 5% increase in the likelihood of companies filing patents.

"Without research tax credit, we would not have been able to enter the global HealthTech race today," insists Christian Pierret, former French Minister of Industry, who helped create it. Patent-box schemes have been adopted in other European countries such as Ireland, Belgium and the Netherlands, where companies can now deduct 80% of net patent income from their taxable base.

Moving Beyond Borders

In Brussels, the Horizon 2020 program is spearheading this innovation strategy through a collaborative approach. In 2008, it led to the creation of the European Institute of Innovation and Technology (EIT), which has resulted in the field in various innovation communities, including EIT Health. This consortium of more than 140 partners from large companies, including Sanofi, research centers and universities in 15 EU countries, enables companies to overcome the fragmentation of the different national healthcare systems and accelerate market access for their products. "Our approach, directly inspired by MIT's innovation model in the United States, is based on the knowledge triangle linking research, education and business creation," explains Jean-Marc Bourez, Managing Director of EIT Health France. Among the thirty or so projects under way, the MD cites EHR2EDC, which aims to collect clinical data from a number of European hospitals in order to develop a system capable of improving the efficiency of medical research. These include the start-up Custodix N.V., a subsidiary of American firm TriNetX, the 12 de Octubre Hospital (Madrid, Spain), and the Hannover Medical School (Hannover, Germany).

"Without research tax credit, we would not have been able to enter the global HealthTech race today."
Christian Pierret, former French Minister of Industry

"Our approach, directly inspired by MIT's innovation model in the United States, is based on the knowledge triangle linking research, education and business creation."
Jean-Marc Bourez, Managing Director of EIT Health France

EuropaBio, another facilitator of collaboration in Europe, is the leading biotechnology manufacturers' association. "We are aiming to be the best possible partner among our members, the European institutions and all the other stake-

"Europe is wonderful in its diversity, but it gives industrialists the image of a fragmented market, in terms not only of regulatory issues, but also of cultures, approaches…"
Joanna Dupont-Inglis, Secretary General of EuropaBio

"Of course, the European environment is less mature than that of the United States, but this also means that there are still very many opportunities here together with the opportunity to create more."
Ivana Magovcevic-Liebisch, Executive Vice-President, Chief Business Officer of Ipsen

"It is no coincidence that the United States and China are buying up many of our companies. If we are to hang onto them, we need to take them to the next level. And it is also the role of investors to become involved in the creation of this ecosystem and in the development of products."
Antoine De Lachaux, Investment Officer at the European Investment Bank

holders involved. Europe is wonderful in its diversity, but it gives industrialists the image of a fragmented market, in terms not only of regulatory issues, but also of cultures, approaches, ... There is thus much work to be done to explain the challenges and opportunities within the sector. The European Parliament, which underwent a profound renewal in the last election, is at the heart of this process today," explains Joanna Dupont-Inglis, Secretary General of EuropaBio.

A Recognized Ecosystem

For Ivana Magovčević-Liebisch, Executive Vice-President and Chief Business Officer of the French firm Ipsen, working in Europe can be more motivating than in the United States. "Of course, the European environment is less mature than that of the United States, but this also means that there are still very many opportunities here together with the opportunity to create more." One third of the world's top universities are in Europe and EU researchers produced 28.1% of global publications in 2016, ahead of the US (19.3%) and China (17.7%). "But we still lack the ability to turn basic research into patents, with an entrepreneurial spirit. This is why we need people seeking to bring innovations to patients around the world."

"We have world-class expertise and centers of excellence for basic research and early clinical development programs," confirms Antoine De Lachaux, Investment Officer at the European Investment Bank. "So it is no coincidence that the United States and China are buying up many of our companies. If we are to hang onto them, we need to take them to the next level. And it is also the role of investors to become involved in the creation of this ecosystem and in the development of products."

Innovative Financing

The European Investment Bank (EIB) has established itself in recent years as the financial arm of the Investment Plan for Europe (the 'Juncker Plan'). For example, at the end of 2018, it granted a €30 million loan to medtech firm Carmat, designer and developer of the world's most advanced total artificial heart project. And the same amount was advanced last March to the Irish company Aerogen, which specializes in aerosol drug technologies. This is a real response to the financial needs of companies that are approaching the market, but which are still struggling to find funding in excess of 10 million euros for their final development phases.

The EIB, which can provide funding of up to 50 million euros, has no hesitation in innovating, tailoring its financing methods to actual company needs. "We offer financing in the form of venture debt. It is a hybrid financing tool poised between equity and debt. This debt component must be repaid by the company. But given the risk associated with innovative companies, we also have to capture some of the value when the project is successful. We therefore propose a very flexible structure that avoids dilution of equity fundraising," continues Antoine De Lachaux.

Being able to count the EIB among its investors is also a guarantee of quality for companies, enabling them to attract new investors. Hence the idea of extending this support to companies in their early stages. Last March, the Commission announced the creation of the European Innovation Council, with a budget of 2 billion euros over two years. In partnership with the EIB, its mission is to support pathfinder projects through to the stage where they can attract private investment themselves, with tickets of up to 15 million euros.

Specialised Funds

Another financial innovation is BPI France, which offers a comprehensive range of solutions for the funding of innovative companies, with non-dilutive early-stage financing for collaborative projects, but also for more mature companies, to assist them during industrialization or scale-up.

"Today we invest just over 100 million euros each year in the life sciences through venture capital funds," says Thibault Roulon, Investment Director at BPI France. Earlier this year, the bank presented its new investment fund, InnoBio 2, dedicated to biotech and big data and artificial intelligence technologies adapted to health issues. With 135 million euros, the fund is supported 49% by BPI France and 51% by industrialists within the sector: Sanofi, Boehringer-Ingelheim, Ipsen, Takeda and Servier. But beyond its financial contribution, it is the expertise of the fund that Thibault Roulon emphasizes. "These large medical firms around the table have the opportunity to contribute and help companies and investors. They give management advice on what to do and what to monitor. It's a great program." And it moves forward without wasting a moment: InnoBio 2 has thus already participated in an initial fundraising round of 13 million euros to finance the development of the nanodrug AguIX® from Lyon-based biotech NH TherAguix, which has a wide range of action anticancer drugs. ■

Fabien Nizon

European Solutions for the Transformation of Digital Healthcare

Digital transformation is revolutionizing health systems. There are many opportunities, as well as many challenges, ahead of the European Commission.

The opening up of health data in Europe, a real boon for artificial intelligence and machine learning, is accelerating convergence between health and digital innovations. The databases of European countries, with their centralized systems, are probably among the most replete systems in the world. However, they face intra-community barriers for lack of a common technical standard to simplify exchanges. "We need a Europe that can bring all the players together. On their own, EU countries will not be able to enter a competition that is now global. The battle is not between Germany and France, but between the United States, Europe and Japan. And we won't be able to really impose ourselves without stimulating collaboration in order to reach critical size," explains Jean-Christophe Tellier, Chairman of the Innovation Board, EFPIA, and CEO of UCB Pharma.

"The battle of artificial intelligence is not between Germany and France, but between the United States, Europe and Japan." Jean-Christophe Tellier, *Chairman of the Innovation Board, EFPIA, and CEO of UCB Pharma*


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"The European Electronic Health Record exchange format will enable a common technical specification to be put in place and remove barriers to a single digital health market." Isabelle Jégouzo, *Head of the European Commission Representation in France*


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Common Standards

This problem has been earmarked by the European Commission, which recommended the European Electronic Health Record exchange format last February. "This format allows for the establishment of a common technical specification and removes barriers to a single digital health market," says Isabelle Jégouzo, Head of the European Commission Representation in France. The text discusses different types of data, such as laboratory results, medical imaging files and reports, as well as hospital discharge reports.

This is an essential simplification not only for data scientists but also for European citizens. By the end of the year, seven European countries will thus be able to consult the shared-access medical files of patients from other EU member states via the "My health @European Union" platform, a new infrastructure that also facilitates cross-border e-prescription and has already been implemented in several countries.

Another initiative of EU member states is the European '1+ Million Genomes' Initiative. Signed by 22 countries, it aims to make at least one million sequenced genomes available to EU researchers by 2022.

Well-Recognized Need for Investment

Finally, the digital transformation of healthcare requires significant financial investment. This is a difficult burden for states to manage at a time when health systems are already under increasing financial stress. "This is why the Commission wants to ensure that the next Financial Framework, currently under discussion, is able to support these projects." A number of budgets are already in contention. The Digital European program, which is involved in the deployment of digital technologies in healthcare, is expected to receive a budget allocation of EUR 9.2 billion for the period 2021-2027. Five priority investment areas have been identified: supercomputers, artificial intelligence, cybersecurity, digital skill building, and access to these solutions within the European territories.

Not to mention the European investment program Horizon Europe 2020, which is expected to be redeployed over the period 2021-2027 with a budget of 100 billion euros, or the Juncker Plan, which encourages investment in innovative companies. "We are also relying on private investors to support these European projects. They will benefit from the support of the European Commission. The transformation of healthcare through the meeting of patient needs offers great opportunities for investors." ■

Fabien Nizon

Keys for Tackling the Future of Innovation

"Significant progress was made in our understanding of genome function and in the development of innovative medicines through biotechnology. In this new ecosystem of innovation, start-ups are key partners for pharmaceutical companies", introduced Thomas Borel, LEEM's director of scientific affairs, ahead of a roundtable discussion with Frédéric Collet, Chairman of LEEM and Jean-Christophe Tellier, Chairman of the Innovation Board, at EFPIA.

"There is no innovation if patients do not have access to the medicines they need."
Frédéric Collet, Chairman of Leem & Chairman of Novartis France


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"From the patient's point of view, the whole healthcare system is organized in a very vertical fashion. It's exactly the same viewpoint that start-ups have of the healthcare market."
Jean-Christophe Tellier, Chairman of the Innovation Board, at EFPIA & CEO of UCB Pharma


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The Future of Innovation

● **F. C.** Medicines derived from living organisms and the use of new vectors of innovation are paving the way forever greater therapeutic advances between now and 2030. This is one of the main conclusions of our prospective study Health 2030*. But while we are used to talking about medical and scientific innovation in the pharmaceutical industry, going forward it is no longer the sole topic. Digital and technological tools have a lot to contribute, especially on patient pathways. Drug companies have considerable expertise in this area. We know the potential of these tools and we have new resources, with millions of clinical patient data sets. Not to mention that we visit about 100,000 doctors a day. That is incredible potential!

The European ecosystem

● **J.-C. T.** The European contribution provides an essential accelerator. I will give two examples: the first is the Innovative Medicines Initiative (IMI), which is the largest public partnership. Since it was launched 10 years ago, 121 projects have been jointly funded by the European Union and EFPIA members, including pharmaceutical companies. The result is excellent, with more than 4,000 publications over this period. The second example is the LifeTime Initiative. This is a European consortium launched in 2001, which receives funding from Horizon Europe. It brings together 120 scientists from across Europe and more than 60 companies, with the aim of modeling and better understanding the link between genomics and phenotype.

Towards a Patient-Centric System

● **J.-C. T.** From the patient's point of view, the entire healthcare system is organized highly vertically. Patients must go to their GP, then one specialist, and then a second, with no connection between the three players other than the patients themselves, who ultimately constitute the sole link in their own care process. We therefore need to create the necessary connections between all stakeholders, to provide the best possible treatment and therapeutic strategy. This is the same viewpoint that start-ups have in the healthcare market. They also find themselves confronted with different components, actors working in silos, when what they need is to work together at the right moment.

● **F. C.** The patient must be at the core of our work. Today, 75% of patients expect to return home during treatment. New tools must be developed to facilitate their treatment and ensure good compliance on their part.

Essential Collaborations

● **J.-C. T.** Obviously, it's easy to lay down the law that we must work together. But it is quite another thing to build trust between partners who have no experience of this approach. First, we need to create opportunities, to bring different experts together around the same table and to then move forward little by little. It takes 10 years to create solid collaboration around a platform where everyone is working together.

● **F. C.** We must look at the legacy of our industry. We have learned for years to invest massive amounts in very long-term projects while controlling risk. Now everything is moving a lot faster. Start-ups have insight, energy and the ability to decipher these new issues that we do not have. We need to move towards a much more collaborative model where we are not in control of everything and where we must take risks.

Fabien Nizon

(*) HEALTH 2030: A Forward-Looking Analysis of Health Innovation (published in French: SANTÉ 2030 : une analyse prospective de l'innovation en santé)

What Funding for the HealthTech Industry?

Lack of funding is a chronic problem for European HealthTech firms. Although in the past, they had no choice but to go public, often prematurely, they can now rely on more active investors who provide a toolbox suited to each stage of company development.

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Over the past two years, investments in HealthTech companies around the world have risen sharply. However, Europe has benefited only partially from this trend. In 2017, the global amount of funds raised in the HealthTech sector (via venture capital and IPOs) reached a record level of €26 billion (source: EY). Of this sum, only €6.2 billion went to European companies, equivalent to just under a third of the funds raised in the United States (€19.8 billion).

However, according to funding experts, the picture is not so bleak. "Financial resources are available in Europe. We sometimes hear that it is impossible for a company to raise more than 100 million euros in Europe through venture capital funds. There were no such transactions in 2017, but three were carried out in 2018 and there have already been four in the first half of 2019, two of them in France; medical appointment specialist Doctolib (€130 m) and biotech firm Ynsect, which specializes in agri-food (€110 m)," points out Olivier Garnier, Founder and Managing Partner at Bryan, Garnier and Co.

The second half of the year even began at a new European record high, with the raising at the beginning of July of $325 million by German biotech BioNTech AG, which specializes in the development of personalised cancer therapies. "To accelerate this movement, what we need now is more banks, better funds and executives who can withstand the pressures to build the environment. But we already have the right science. I am very optimistic and looking forward eagerly," continues Olivier Garnier.

A Funding Chain

The creation and development of a health company involve several phases. Seeding is simplified in Europe by many public schemes, such as

tax credits and the support of public investment banks. These devices allow many researchers to move their work from the fundamental research stage to explore product the feasibility. The first funding round tables (rounds A and B) are then organized without difficulty for the most innovative projects. Although funding is lower, by around 10 million euros on average, it has doubled over the last ten years.
"Overall, non-dilutive funding needs at early stage are well covered. There are indeed some very encouraging initiatives in Europe," says Cédric Moreau, Partner at Sofinnova Partners. "Nevertheless, there still remains a hurdle to be crossed. For companies, this is the time when research, R, must be transformed into development, D. It is a completely different story and it can be difficult for leaders who have conducted the academic research to succeed in this transition." This passage requires significant funding, with Phase III trials, the last step before marketing authorization, costing between 50 and 150 million euros.

More Specialized Banks

Financing the capital of an innovative company, particularly in the healthcare sector, is the business of private equity and venture capital companies. However, some banks invest in seed funding and develop a specialized offer. At BNP Paribas, for example, an 'innovation center' was launched in 2012. Dedicated to start-ups, "it brings together a hundred bankers for about 3,000 corporate clients. They understand their clients' needs, their environment and their difficulties," explains Sophie Pierrin Lepinard, Healthcare Investment Manager with BNP Paribas Development. "This activity is then completed by investment activities, as well as mergers and acquisitions, fundraising and IPOs."
Société Générale has also set up a reference team to support innovative companies from the very beginning. "Health start-ups, which have no revenue and spend a lot of money on product development, are not the usual customers for traditional banks. This is why they are handled by dedicated experts who understand the challenges facing the sector. There is also the possibility of teaming up with Corporate Banking," explains Delphine Le Louet, Equity Research Senior Analyst, Biotech/Medtech and European Healthcare at Société Générale.

"What we need now is more banks, better funds and executives who can withstand the pressures to build the environment."
Olivier Garnier, Founder and Managing Partner at Bryan, Garnier and Co

"Early internship funding needs are well covered. But there is effectively still a hurdle to get over. For companies, this is the time when research, R, must be transformed into development, D."
Cédric Moreau, Partner at Sofinnova Partners

Venture Capital, at the Heart of Risk

The aim for Europe and its companies is now to gain visibility and attractiveness among a wider base of international investors and to diversify the types of financing according to their maturity. Private equity primarily funds companies that have reached a certain level of maturity. Venture capital funds, on the other hand, support new companies, including innovative start-ups. The risk to the investor in this instance is very high, which pushes the funds to seek out the "rare pearl" offering exponential growth potential.
"At Sofinnova, we pay close attention to the company management. Even though there may be innovative scientific promise, the sector is very competitive, and you have to be able to execute a plan, manage research and development and intellectual property, manage the company's talents, know how to talk to regulators and prepare access to the market," explains Cédric Moreau. "Then we need to see clearly how the company proposes to create value. Is it a completely disruptive product that will meet hitherto unmet medical needs for example? Finally, we position our investments over a four-to-five-year horizon. The entry point into the company is essential, but it is also important to anticipate the exit point, and to implement this at the best time."
This is a crucial period when the company establishes the credibility of its project and has greater visibility, ensuring a rewarding exit for its investors and sometimes even its founders. Investors or a foreign group, often American, then maneuver to buy up the company's assets. But this approach often heralds a shift of the company's business to the other side of the Atlantic, to develop in the American market, which is consistently more profitable than Europe.

The Poor Start of French Biotechs on the Stock Exchange

Unable to find the necessary funding for their development, a lot of healthtech firms, mainly French, went public in the mid-2010s, despite being in the early stages of their work. The proliferation of transactions, and of failures, has cooled the ardor of investors. "There was too much amateurism. The statistics are terrible. Over the past decade, 50% of biotechs listed on the U.S. stock exchange have seen their share prices rise. In Europe, meanwhile, 85% of stocks are down!" laments Olivier Garnier. "A lot of mistakes have been made. HealthTech companies need to stay away from public procurement for longer until they can actually deliver results."

"Health start-ups, which have no revenue and spend a lot of money on product development, are not the usual customers for traditional banks."
Delphine Le Louet, Equity Research Senior Analyst, Biotech/Medtech and European Healthcare at Société Générale

"Today, the problem is not to attract more public money in Europe. It is time to create a virtuous circle with investors and to be able to mobilize five to six specialized funds for these transactions."
Marc Le Bozec, Private Equity Fund Manager at Arbevel Financial

Hence the importance of quickly establishing a strong and varied investor syndicate, so as to avoid dependence on a single resource. "To complete a transaction in excess of 100 million euros requires the involvement of American investors. Today, the problem is not to attract more public money in Europe. It is time to create a virtuous circle with investors and to be able to mobilize five to six specialized funds for these transactions," says Marc Le Bozec, Private Equity Fund Manager at Arbevel Financial, who is hoping for rapid new industrial successes in Europe that will attract general investors to the sector. "The trend is positive, as may be seen in Belgium, with companies like Galapagos and TiGenix. In France, the success of companies such as DBV Technologies or Genfit represent a major event for the sector." Experts also rely on more active European investors, including Sofinnova, Andera Partners and Kurma Biotech, who have the ability to put higher amounts on the table.

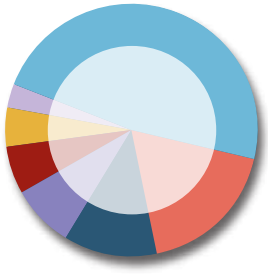
New Players

"Companies need to use the right investment tools at the right time," says Alain Decombe, Paris Managing Partner at Dechert LLP. "These range from public financing and venture capital to the early stages of IPO at the end of the cycle. But there are other tools that can be used at any time during development, such as partnerships. We are now seeing more and more large companies struggling to find innovative drugs who are looking at start-ups to reorganize their pipelines, in some cases even at the preclinical stage."
New categories of investors are also entering the sector. Generalist and crossover funds, which hold both public and private equity investments, such as Innobio in France, are becoming more active in the emerging biotech sector, even at the early stages. Chinese investors, such as 6 Dimensions, Hillhouse and Sequoia China, are also on the lookout for innovative companies, with the aim of expanding their business in Asia but without abandoning their domestic market. "We are also starting to see individual investors, billionaires, turning up, and they themselves are becoming institutional investors. It's a real trend," adds Lilian Stern, Principal at Stern IR.

Ticking the Stock Exchange Boxes

The entry of HealthTech firms onto the Stock Exchange is the next reward for proof of feasibility of the product under development. Several conditions must be met. "A biotech must have at least one drug in phase II. For MedTech firms, the situation is different, since it is usually a question of financing the industrialization and commercialization phase," explains Éric Forest, who warns against haste in this process. "An IPO should not be simply a recourse against bankruptcy. The candidate company must have at least 12 months' financial visibility."
"A company capable of achieving a valuation of 200 million euros or dollars at the time of its IPO will be able to raise sufficient capital and create adequate value," adds Robert Berger, Managing Director, Head of Healthcare Equity Advisory at Rothschild and Co., recalling that there are now more than 600 biotech firms listed in the United States. "In this industry, you are constantly fighting to stay on the investors' radar and keep the door open for access to the post-IPO market."
Experts also stress the need to find the right partners to assist in stock market entry. "For each IPO, we contact about 80 investors, about 30 in the United States and a dozen in the main European markets: the UK, Belgium, France, the Netherlands and Germany. Gaining their trust is an important and essential job," says Olivier Garnier. This approach guarantees the upstream purchase of a large propor-

GEOGRAPHICAL SOURCE OF CAPITAL INVESTED IN EUROPEAN LIFE SCIENCES COMPANIES
As a % of assets under management



- 48 % United States
- 6 % United States Other
- 18 % France
- 5 % Norway
- 12 % United Kingdom
- 3 % Germany
- 8 % Belgium

Source: Euronext on 31/10/2018,
EY - Panorama France HealthTech 2018

Hong Kong, a New Competitor to the U.S. and European Markets

As the world's third largest financial center, Hong Kong has long remained inaccessible to innovative companies without income. A change of the rules in April 2018 now means they have easier access to the market. Several biotechs, mainly Chinese, have benefited from these new provisions, including Ascletis, which is developing a hepatitis C treatment. This is an ambitious gamble for Hong Kong, which still suffers from its lack of expertise in the sector. Although the city has only about 20 bankers specializing in biotech, it now hopes to take full advantage of China's booming health industry.

tion of shares placed on the market, while reassuring individual investors also subscribing to the transaction. In 2018, for example, MedinCell, a biotech developing innovative solutions for drug injection, entered Euronext Paris with the support of its investors and partners: CM-CIC Innovation, BNP Paribas Development, Seventure Partners and Teva, who at that time had purchased 20% of the new share issue.

However, in keeping with these unspoken rules, Isabella Schidrich, Senior Managing Director at the Nasdaq Stock Exchange, believes that they can be adapted to each company. "The key point is a company's growth opportunity. If it already has a strong equity story, high quality management and an effective story to win over investors, then it can go public at any time."

" We are also starting to see individual investors, billionaires, turning up, and they themselves are becoming institutional investors. It's a real trend."
Lilian Stern, Principal at Stern IR

"A company capable of achieving a valuation of 200 million euros or dollars at the time of its IPO will be able to raise sufficient capital and create adequate value."
Robert Berger, Managing Director, Head of Healthcare Equity Advisory at Rothschild and Co

The Life of Listed Companies

However, going public for a health company is not simply a matter of raising broader funding. Entering regulated markets means it now faces the scrutiny of financial analysis firms. Above all, the long research and development times do not always coincide with those of investors, especially individuals who expect regular development within the company. "Having a news flow that can really hold investors' attention and keep them eager once the company is in the marketplace is essential. The death knell for a listed company is a failure to communicate adequately then seeing its share price fall 30% six months after the entry," warns Olivier Garnier.

This is especially true since a HealthTech firm's need for liquidity does not stop when it goes public. On the contrary, the final stages of product development are often the costliest. In Europe, listed companies completed 2,213 post-IPO financial transactions in the first three quarters of 2018, representing more than 40% of capital-raising operations recorded over the period. Although a complex circuit, it is now essential for the future of HealthTech in Europe. ■

Fabien Nizon

Winning Together: Successful Corporate and Start-up Collaborations

Faced with the complexity and long timeframe of medical research, large pharma companies are busy multiplying partnerships with specialized research laboratories. These essential collaborations also enable them to invest in new areas of innovation, such as the digital and prevention areas of healthcare.

In the healthcare industry, large companies are now product developers rather than simply product discoverers. "Today, at Boehringer Ingelheim, half the products in our pipeline are linked to external innovation through partnerships and collaborations. Our priority lies in certain therapeutic areas, including cardiometabolic diseases, respiratory diseases, immunology, central nervous system diseases and oncology. But it is also the new technologies that allow us to accelerate development and clinical trials and thus enhance access to the therapeutic market," explains Dr. Emilio Erazo-Fischer, Global BD and Licensing Oncology at Boehringer Ingelheim.

In particular, the German firm has teamed up with the French biotech OSE Immunotherapeutics to develop a cancer treatment, drawing on its expertise in immunology. "From the outset, we decided not to hamper OSE's work and thus not to transfer the research program. In this way, just nine months after signing the partnership, we obtained a Clinical Trial Authorization (CTA) and the first patients were included in Phase I in June."

At the Heart of Efficient Care

Strengthening prevention and efficiency of care now lies at the heart of health policies. This shift of priority allows healthcare manufacturers to enter the sector at the care management level. "Pharmaceutical companies have excellent medicines. But this is no longer enough. Finding patients who need access to these treatments is even more important," says Patrick Dey, Amgen's Vice President of Digital Health and Innovation.

In particular, the American group has signed a partnership with Owkin. This company is developing an algorithm, which, through data analysis, prevents a second or third heart attack in patients with a history of initial infarction. "We hope that with their digital expertise and treatments for cardiovascular disease, we will be able to reach many more patients than we do today." A vision shared by Jean-Frederic Petit-Nivard, Owkin's Pharma Development Director. "Today we are seeing more and more drugs coming on the market. The challenge is to ensure that they reach the right patients and meet medical needs. To achieve this, we need the leverage of new technologies. This is what we're doing with Amgen today."

Multiple Partnerships

At the heart of the medicine of the future, from diagnosis to patient assistance, artificial intelligence is also being constructed through partnerships between engineers, industrialists and healthcare professionals. The French company Diabeloop is developing a new tool, DBLG1, which automates the treatment of type 1 diabetes. Sometimes compared to an "artificial pancreas", this innovation, based on artificial intelligence, is primarily the result of a historical collaboration with CEA-Leti in Grenoble, which enabled the development of the technology.

"Once we proved its efficacy, we looked for other partners among technology solutions providers. To function, the device requires an insulin pump and a sensor that we do not manufacture. Working together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"Today, at Boehringer Ingelheim, half the products in our pipeline are linked to external innovation through partnerships and collaborations."
Dr. Emilio Erazo-Fischer, Global BD and Licensing Oncology, Boehringer Ingelheim

on such an innovation is sometimes complicated, but we have been able to obtain CE marking and to conduct very successful clinical trials," said CEO Marc Julien. "We are now moving towards commercialization of the device and we are once again seeking new partners, mainly home-care providers."

Becoming a Partner in the Ecosystem

In order to avoid being surprised by innovation in healthcare, especially in the digital area, the large pharma companies carefully scrutinize the work of start-ups. They even employ authentic "innovation hunters", scientists who meet health start-ups in search of promising molecules or solutions. However, targeting is complex given the multitude of players and the fierce competition. Hence the value of deploying Innovation Hubs in the most efficient ecosystems. All major pharma companies, including Pfizer, Sanofi and GSK, have developed incubators of this type in recent years.

French firm Ipsen, which does not have the clout of these giants, has for its part teamed up with BioLabs, the first start-up incubator in the United States. "Ipsen has undergone numerous transformations in recent years. In particular, we decided to build on our strengths, drug development and commercialization, by doing away with some of our research activities. Rather than parting with our Cambridge laboratories, we decided to make them accessible to start-ups through a partnership with BioLabs," points out Veronique Riethuisen, Senior Vice President, Global Head of Business Development and Alliance Management at Ipsen.

Ipsen now shares this space with these companies, of whom there are around 15 today. "They have access to our scientists, but also to our entire business organization, via training sessions in the fields of clinical research, regulatory issues and market access. Criteria have been pre-defined by Ipsen and BioLabs to help select the most promising companies. However, both partners remain very flexible," continues Veronique Riethuisen. "Oncology is our preferred area, but we are also open to other therapeutic fields and to artificial intelligence. We are talking about early science, so we do not know what future needs and innovations will be."

"Pharmaceutical companies have excellent medicines. But this is no longer enough. Finding patients who need access to these treatments is even more important."
Patrick Dey, Vice President Digital Health and Innovation, Amgen

"Rather than parting with our Cambridge laboratories, we decided to make them accessible to start-ups through a partnership with BioLabs."
Véronique Riethuisen, Senior Vice President, Global Head of Business Development and Alliance Management, Ipsen

Moving Beyond a Single Model

These partnerships allow the pharmaceutical industry to direct and expand the provision of services centered around drug treatments. This is an indispensable "beyond the pill" strategy for patients, whose treatment is now migrating out of hospitals and into the primary care sector. This trend also applies to other sectors, such as insurance.

With its new subsidiary Axa Next, dedicated to innovation, Axa is seeking, for example, to develop business models and new services "beyond insurance" in a partnership approach, explains Fanny Pouget, the French insurer's Group Innovation Head of Operation. "Healthcare is a strategic priority for Axa Net. We are supporting the development of start-ups through different vehicles and dedicated teams such as Kamet, a structure dedicated to the creation of innovative companies that now has very promising companies in its portfolio, particularly in the teleconsultation sector. There is also AXA Venture Partners, which invests in technologies dedicated to insurtech, especially in digital health."

Complex Partnerships

However, like any marriage – an analogy that pops up regularly in the experts' discourse – these partnerships need a strong commitment from both sides to succeed. "It's not always easy. For example, the due diligence processes on which large pharma firms insist are difficult to carry out and tedious," says Alexis Peyroles, CEO of OSE Immunotherapeutics. "But the questions we are asked also provide us with clues about the expectations of these firms and a better understanding of the type of partnership they are looking for. You have to be able to answer these questions, to look very closely to make sure you also have the right partner to successfully navigate the many product development checkpoints."

For companies that increasingly rely on partnerships, success is not just about investment. So how do we ensure that value creation is maintained in the long term? "Signing a contract is not an endpoint, but a beginning. Everyone can be happy to work with their partners of choice, but the final proof comes from the work actually done, development of the product and how this relationship evolves over time. To ensure the best possible chance of success, I can only advise both sides to pay attention to due diligence and how their partners make their decisions. This period of negotiation is essential. Any difficulties at the outset are certain to continue throughout the partnership," warns Veronique Riethuisen. ■

Fabien Nizon

Maryvonne Hiance: "Coming Together to Build Europe's HealthTech Ecosystem"


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More than simply a conference on Financing HealthTech, the first HealthTech Investor Days provided an impetus for strengthening the European ecosystem. On the Old Continent, the sector is indeed younger and less mature than in the United States, and much building still remains to be done. But the foundations are solid: all the actors who spoke during these two days were keen to welcome medical research in Europe, supported by the quality of its experts, universities and public research organizations.

This dynamism is today reflected in 3,000 European biotechnology companies and more than 25,000 medical technology companies. They are each carrying forward a medical innovation that they are keen to make available to patients at the earliest possible date. Some are already very successful, with 14 European biotech firms now having a valuation of over one billion euros. These are unicorns that shatter the myth of the need for European firms to cross the Atlantic to reach their true potential.

By bringing together for these two days 90 European HealthTech companies, almost as many international investors, from the United States, China, Singapore and Israel, among them large funds such as Orbimed, Temasek, Cathay Capital, and so on, as well as pharmaceutical groups, scientists and industry experts, we have created a privileged meeting space.

This is what we were missing in Europe: a true "accelerator" offering investors a unique opportunity to discover the European ecosystem and forge links with its most mature companies, while enabling pharmaceutical companies to identify the most promising technologies.

HealthTech Investor Days is now a must-attend annual event in Europe, in the same vein as the annual JP Morgan conference in San Francisco. ■

Maryvonne Hiance

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Olivier Chabanon, General Delegate of France Biotech:

"HTID has Received Strong Support from the French Government"

Olivier Chabanon, General Delegate of France Biotech, was instrumental in organizing HTID with his team (Chloé Evans, Marion Garbay, Sophie Villedieu) and his predecessor Didier Géneau. He offers a very positive assessment of the event, which has now become an annual must-attend event for the sector.


DR

How did this event come about?

● The decision to set up HTID was made after last year's success at the BIO International Convention in Boston. We took 20 French and five European companies to meet some 20 American investment funds and witnessed positive contacts. So we thought why not do it in Paris? There is a clear opportunity to host such an event in Europe, as London prepares to leave the European Union. Admittedly, organizing HTID was quite complicated at first. We met with different associations in the health sector and noted the lack of European cohesion. Then, as the event began to take on visibility, everything started moving quickly. In the end, the enthusiasm it generated completely exceeded our expectations.

What do you see as the key points to take from this first edition of HTID?

● First of all, there was the participation of investors from the USA, Japan, Singapore, and elsewhere. These were not financial intermediaries, as we sometimes see in San Francisco, with whom discussions are not always constructive. During THID, companies really had direct access to these internationally renowned fund makers through one-to-one meetings, with the opportunity to take things further afterwards. This is exceptional for the sector. Of course, we would have liked to have had even more, but it is a real success for a first event. Today, SMEs in healthcare, in France or Europe, really struggle to raise more than 50 million euros to finance the development of their products. And the attendant risk is that they will lose not only their innovation but also their foothold in the sector. This is why we need to mobilize as many investors as possible. The participation of large pharma firms has also been extremely welcome. They too were able to interact with biotech executives and forge links that will surely be strengthened in the future.

Are you satisfied with the institutional support you received for these days?

● Yes, HTID received strong support from the French government. The event was placed under the high patronage of the President of the French Republic, Emmanuel Macron, with sponsoring by the Minister of Economy and Finance, Bruno Le Maire. We were also received, together with a delegation of participants, at the Hôtel de Matignon for an institutional evening on June 24, in the presence of Secretary of State Agnès Pannier-Runacher. Such support really illustrates the commitment of the public authorities to this initiative by France Biotech, and, more broadly, to the development of HealthTech in Europe. The attractiveness of Europe highlighted by HTID also found an equally favorable to echo throughout the European institutional ecosystem. The presence of the Head of the European Commission's representation in France, Isabelle Jegouzo, representatives of the European Investment Bank, and European associations such as Europa Bio, EIT Health, EBE (European Biopharmaceutical Enterprises) and IREFI (Economic Institute for Relations France Italy) is just one example of the rallying of the European ecosystem around HTID.

France Biotech has just announced its next edition in 2020 in Paris. What are the goals?

● The second edition of HTID will be held on 22 and 23 June 2020, again in Paris. We want to continue this excellent momentum. The goal is clear: to bring in more foreign investors, especially European investors, and to organize numerous high-quality exchanges. We are aiming to make HTID the major European HealthTech event, modeled on the JP Morgan Healthcare Conference in the United States, but on a more human scale and at a more reasonable cost!

Interview by Fabien Nizon

Amgen is a value-based biotechnology company, deeply rooted in science and innovation to transform new ideas and discoveries into medicines for patients with serious illnesses.

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Partnering Towards Success

Serge Weinberg, Chairman of the Board of Directors of Sanofi, and Hervé Brailly, Chairman of Innate Pharma, take stock of their cooperation in the field of immuno-oncology and highlight the importance of partnerships in the pharmaceutical sector.

"We need to be stimulated by the speed of smaller companies with limited resources and no time to waste."
Serge Weinberg, Chairman of the Board of Directors of Sanofi

"Biotech teams are ultimately far more stable than those of big pharma."
Hervé Brailly, Chairman of Innate Pharma

Are Partnerships the New Accelerator of Medical Research?

● **S. W.** They form a crucial element for the future of the pharmaceutical industry. Nothing can be done without the ability to work alongside the right companies. Innovation has accelerated in recent years, and as a group, we must recognize that we do not have the capacity to move as fast as biotech. This is particularly true since we are no longer talking simply about the very long road that must be built between science and medicine, but also about everything that goes "beyond the pill". Thus, the scope today is not confined to science, but also concerns how to improve treatments and links with patients with the help of digital support. This is an area where the pharmaceutical industry has ground to make up, while new players move in, such as Google, with whom we have a partnership.

● **H. B.** Partnership is the key factor in building a biotech firm. The process starts with a research and development agreement. The company then gains maturity. Product development continues and the next step is to obtain validation from a pharma company through a licensing agreement. That is what we have achieved, and it is precisely this that has transformed our business. We have gained visibility in the US market and with investors. In our third partnership, signed in 2015 with a large pharma company, we were able to keep part of the rights to the product. Finally, our fourth agreement allowed us to take back a product from our partner's portfolio. Our goal is now to attract more products and become a fully integrated company specializing in niche oncology products.

Partnership on a Day-to-Day Basis

● **H. B.** Partnership is not just about funding. It is also an opportunity to find out not just about our partner's structure and about the constraints of working together, but also how to turn research into a product. While it may not necessarily be easy to work with a pharma company over the long term, it is really crucial to the structuring of a biotech firm and to the adjustment of its strategic vision at different stages of development.

● **S. W.** It is difficult to drive innovation in large groups, which can sometimes be highly bureaucratic. We need to be stimulated by the speed of smaller companies with limited resources and no time to waste. They bring us the responsiveness and organizational model we need to work more transversally.

Keys to a Successful Partnership

● **S. W.** There are many conditions, but there is no one-size-fits-all formula. Each agreement is tailor-made to very specific subjects backed up by the necessary resources. You have to follow a schedule and be ready to give up quickly if things don't work out. We cannot waste time multiplying partnerships in the absence of tangible results. There are other pitfalls that must be avoided. Sometimes, for example, pharma companies tend to hitch up the few people responsible for biotech with a team of ten or so interlocutors but with no real responsibility. What is really needed is the ability to adapt the organization as needed, to work in project mode and to acquire a sense of urgency. This approach also reassures our partner of our firm commitment.

● **H. B.** We need to move fast, but not too fast, because we also need to create the necessary structure. It may take one or two years to get to this point and then allow both partners to be more responsive. Biotech needs to understand how pharma companies work, and they must make sure they have a sufficiently high-level contact with the organization to make the big decisions. Often however, the key problem is constant reshuffling within the teams. It is also something of a paradox: ultimately biotech teams are far more stable than those in large drug companies and such turn-over makes it difficult to build relations.

Fabien Nizon

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Investors: Keeping a Close Watch on European Biotechs

At each stage of their financing, HealthTech companies meet with industry experts, investors and manufacturers. This enables them to learn about their environment and adequately meet market expectations.

By investing in HealthTech companies, venture capital funds take a significant risk. Hence the professionalization of their teams, whose mission is to uncover the "rare pearl" in the market offering exponential growth potential. OrbiMed, the largest specialized healthcare fund, with assets of $12 billion, now has offices around the world, in San Francisco, Shanghai, Mumbai and Herzliya, Israel. "We made our first investments in Europe last year. The ecosystem here is very good, especially in genetic research. We are now looking for new investment opportunities, especially in France," explains Nissim Darvish, Senior Managing Director of the company.

Specialized Teams

OrbiMed, which employs around 100 scientific professionals, doctors, and investment specialists, is today extremely positive about the biotech sector. "The number of innovative products in Phase II and III is rising. And health authorities are putting in place programs to speed up approval. Meanwhile, large pharma companies need to reshape their pipelines, with more specific indications. For us, this environment offers a great opportunity. It allows new companies to be built and financed around a product and which will easily find a buyer," continues Nissim Darvish, although he is more reserved about MedTech. "The last two years have been a period of consolidation in the sector. Since the number of companies and buyers is in decline, to invest you have to make sure you have a solid investor syndicate."

In New York, H.C. Wainwright and Co., which specializes in the health sector, relies on an equity research group comprising around ten senior analysts to guide its investments. "We have to understand not only their research work, but also their model and how we can help them bring their agenda to the fore," says Oded N Spindel, Vice President of the investment bank. The expert is also positive about the sector in Europe, where he is pleased to find very competent managers, whom he advises to remain open to their environment: " Some companies are not listening carefully enough to the advice of large drug companies and investors. This is a mistake: you have to pay close attention to make sure you are meeting the expectations of the market." ■

"We made our first investments in Europe last year. The ecosystem here is very good, especially in genetic research."
Nissim Darvish, Senior Managing Director at OrbiMed

"Some companies are not listening carefully enough to the advice of large drug companies and investors."
Oded N Spindel, Vice President of H.C. Wainwright and Co

Fabien Nizon

Synergy between Business and Fundraising

The diversity of financing tools available to start-ups allows them to set up operations that accelerate their business model at the same time.

1. Valneva: a merger to secure production

Valneva, the European leader in biotechnology specializing in vaccines and antibodies, was created in 2013 through a merger between two equals, French firm Vivalis and Intercell in Austria. This type of transaction is quite rare in the sector and was accompanied by a capital increase of 40 million euros. "Intercell has complemented Vivalis' research and licensing activities with essential production skills and development expertise. We must not forget of course, that research and development are two fundamentally different professions," explains David Lawrence, CFO of Valneva. In the biotechnology sector, highly complex production processes are at the core of product value. "Thus, production facilities certified by health authorities, experts, processes and documentation are extremely important elements. This is something that a research company must acquire in order to industrialize its production and scale up." Prior to the merger, Valneva relied for production on external partners, including large drug companies. "But often these partners control all decisions, which undermines the visibility of the company's business." With a turnover of 113 million euros in 2018, Valneva now attracts larger investors. "They are less worried about the risk of manufacturing and product development, which has allowed us to capitalize in the best possible way."

2. In Korea, ToolGen reinvents itself in a new environment

Korean biotech is booming. By increasing aid from the current $2.15 billion to $3.3 billion by 2025, the government is seeking to make the sector a new driver of the country's growth. This represents an opportunity for start-ups like genome specialist ToolGen, which has faced many challenges in recent years: "Despite our team of specialists, we still lack experience in transforming this technology into therapies. Our manpower pool is limited. Also, a few years ago, Korean investors weren't very active with regard to small biotech firms like us," says Jongmoon Kim, CEO of ToolGen. "So we tried innovative approaches through collaborations and open innovation by building a research and development network in South Korea and abroad."

This transformation was further accelerated in June through its merger with its partner Genexine. The resulting biotech, ToolGenexine, now has the teams and funding needed to prepare for the commercialization of GX-H9, a treatment for children with growth hormone deficiency, and to speed up the clinical development of its gene therapy, HyLeukin-7.

3. Servier moves closer to start-ups with the creation of its new Innovation Hub

Servier has set itself the ambitious goal of bringing a new drug to market every three years. "Obviously, to achieve this goal, we need partnerships, and we must become an active player in this ecosystem," says Eric Falcand, VP Global Head of Business Development and Licensing at Servier. The French laboratory has already found its place in Boston, with the creation of Servier BioInnovation, following the acquisition of Shire's oncology subsidiary. "It has been so successful that we are now looking for new locations to set up our research centers, for example in China."

In France, the group laid the foundation stone for its future research institute in Saclay, south of Paris, in June. This project, with an investment of 300 million euros, will allow the laboratory to bring its 600 researchers together at the same site. "Most importantly, the Board of Directors decided to take advantage of this opportunity to create an incubator. This is a key element of our open innovation policy. It will be open to start-ups, which will benefit not just from the infrastructure but also from the expertise of our teams, while retaining their independence". This is a key condition for many young companies, who want to ensure that they create enough value before entering into a partnership.

4. Takeda retains close ties with local innovation

With its acquisition of Shire, Takeda has embarked on a strategic acceleration of its global footprint. Nevertheless, the Japanese group continues to keep a close eye on local innovation. "To this end, we have experts dedicated to seeking out strategic alliances, and academic partners. But there is also Takeda Venture, which is the corporate venture arm of Takeda," explains Julie Puype, General Manager of Takeda France, citing three examples of this approach. The first, with the American Emendo Biotherapeutics, which is developing a platform for genetic modification, started out as an investment. "It allowed us to familiarize ourselves with the company and its teams and it ultimately led to a partnership."

Another example is the partnership with French biotech Enterome, which specializes in therapies for diseases associated with the gut microbiota. Signed in 2016, it evolved in 2018 to a licensing and co-development agreement regarding EB8018, Enterome's most advanced drug candidate for Crohn's disease. Finally, Julie Puype is delighted about Takeda's collaboration with Medtech SIVAN Innovation, which has developed an application that allows early detection by medical teams of sudden relapses of lung cancer via a questionnaire completed by patients on their smartphones. With the help of Takeda, the start-up is now developing this solution in new indications in a clinical trial.

Fabien Nizon

European Strengths in Artificial Intelligence in Healthcare

During a roundtable discussion moderated by François Nicolas, Chief Digital Officer at Guerbet, industry experts hailed Europe's efforts to establish itself in artificial intelligence.

"Regardless of the quality of the algorithms, if the data are not appropriate or not sufficiently representative of the problem being addressed, the results will not be conclusive."
Nozha Boujemaa, Chief Science and Innovation Officer at Median Technologies

"Working in Europe means that we have to have the flexibility needed to meet the specific requirements of each individual country."
Wim Van Hecke, CEO of Icometrix

It is not always easy for patients to trust in machines to take care of their health. However, their overall expectations of artificial intelligence are positive, even if they do not really have any specific knowledge of the subject. "But marked differences exist between generations, even more so than between countries. Thus, American millennials are closer to millennials in France than to the baby boomers of their own country," explains Françoise Simon, Professor at the University of Columbia and the University of Nantes. "Baby boomers are still very much attached to a traditional relationship with their doctor while Dr. Google is now the favorite healthcare professional of young people. For them, the transition to artificial intelligence is very straightforward."

Expectations among doctors are more specific. "Artificial intelligence is well accepted as a means of logistical assistance for administrative tasks such as making appointments. On the other hand, decision-support systems, which are being developed in several specialties such as radiology, meet with some mistrust while diagnostic tools are rejected. According to a survey of 400 doctors, only 19% are willing to co-diagnose or treat patients with the help of artificial intelligence."

Answering Ethical Questions

Faced with the superior clout of the American and Chinese giants, the European Union has decided to focus on the trust and ethics aspects of these new tools. In a report published in April, "Ethics Guidelines for Trustworthy AI", a group of 52 experts (the High-Level Expert Group) appointed last spring by the European Commission has published 33 recommendations. The aim is to establish a framework conducive to the sustainable development of artificial intelligence, while insisting in particular on the importance of including all patients and to preserve the social environment around these programes. In short, patients must not simply be left to their own devices before these machines.

"Great efforts are being made to make artificial intelligence secure. It's not just a question of data, but also of evaluation to ensure the accuracy of predictive models," says researcher Nozha Boujemaa, Chief Science and Innovation Officer at Median Technologies and Vice-Chair of the panel. Certain pitfalls must be avoided: "Sometimes there is confusion between causality model and correlation model, which can create problems in the interpretation of results. Moreover, regardless of the quality of the algorithms, if the data are not appropriate or not sufficiently representative of the problem being addressed, the results will not be conclusive."

However, EU experts are refusing to establish a strict regulatory framework. "The issue is first and foremost one of transparency and traceability. If operators take sufficient care over these two points, regulation will not be necessary," stresses Nozha Boujemaa. In the United States, an FDA-initiated consultation with experts has shown that artificial intelligence is an area of continuous learning, where advances outpace any regulations imposed.

Europe Ahead of the Field?

Investors are primarily focused on artificial intelligence tools that can optimize complex and currently costly processes in the healthcare industries, such as drug discovery and clinical

"Europe has a competitive lead through its workforce. It possesses the key skills in mathematics, modeling and computer science."
Sebastien Woynar, Investment Director at LBO France

"Europe, and France in particular, has undeniable assets regarding access to health data."
Françoise Simon, Professor at the University of Columbia and the University of Nantes

research. "There are three critical elements that place Europe at the forefront and create investment opportunities. First, public funding, which is very high, with organizations such as the BPI in France or its German counterpart KfW. This really allows capital to be directed where it needs to go. Second, Europe has a competitive lead through its workforce. It possesses the key skills in mathematics, modeling and computer science. The third and most important point is the European ecosystem, with health systems that pay for innovation, provided it translates into real medical value. This creates an incentive to target innovation where it is really expected, more so than in the United States," says Sebastien Woynar, Investment Director at LBO France.

"This is an important difference with regard to the United States, where the entrepreneurial culture is different. A company may experience many failures before it finds its market. In Europe, we really want to meet an identified medical need," says Wim Van Hecke, CEO of Belgian start-up Icometrix, a leader in artificial intelligence for brain imaging. "At the same time, working in Europe means that we have to have the flexibility needed to meet the specific requirements of each individual country. This is a real strength for European companies working in the field of artificial intelligence."

According to the director, however, artificial intelligence is only a tool. "Too often we see companies applying for financing simply because they are in artificial intelligence. But this is not an end in itself. In my company, the goal is to help patients with brain diseases. We need reliable tools. It may be artificial intelligence today, but tomorrow it could be another tool."

A head start on data...

Artificial intelligence thrives on data. Provision of access to large medical-administrative bases, whether public or private, thus offers researchers tools to improve the safety, proper use and effectiveness of care. "Europe, and France in particular, has undeniable assets regarding access to health data," says Françoise Simon. "First with centralized databases and dedicated initiatives such as the data hub in France. In the United States, the system is doubly fragmented between hospitals and between insurers. Mount Sinai Hospital in New York, for example, has eight different facilities and 17 different electronic health records (EHR) systems that do not communicate with one another! We expect to have an integrated system by next year."

... but delays in their use

But this head start gained through Europe's nationalized health systems could quickly shrink in the absence of reforms to ensure greater harmonization. In the United States, despite a fragmented market, companies rely in the early stages on the marketing of their product to Medicare and the largest insurers. Conversely, in Europe, each market is treated separately. "Once the green light has been received from the European authorities, it makes no sense for a company to go to the regulator of each country with the same files, the same clinical evidence and the same data. There is clearly work to be done at the European level in terms of common assessment of the clinical value of a product. Today, entrepreneurs are lost, and they are forced to waste a great deal of time and money on such procedures," laments Sébastien Woynar. Other difficulties are commonly mentioned, such as technology transfer, which is more complex in Europe than in the United States, and, of course, it is more difficult to find financing. But even with regard to these issues, experts are agreed on one point: the situation is improving each year. ■

Fabien Nizon

Twenty projects to launch the Health Data Hub in France

In order to accelerate the integration of artificial intelligence into health, France has established a Health Data Hub (HDH), a state-guaranteed technology platform to group together, protect and share health data. "Twenty projects have been selected. They will help us fill out the HDH data catalogue. In addition to health system reimbursement data, we have data from clinical trials, occupational medicine, complementary health insurance firms, etc., in short, everything related to the public health system. But this data will not form a single database. Access will be personalized for each actor, especially if the purpose of the project is of public interest," explains Achille Lerpinière, Head Project Manager at HDH, attached to the Ministry of Health. Some of the projects selected concern drugs. "Ordei" for example will automatically determine the number of patients presenting a given adverse reaction. Others will target specific diseases, in particular cancer with "Deepsarc". This project will seek to determine the most relevant treatment regimen for patients with sarcoma, a rare tumour, but for which France nevertheless has a large base of 50,000 patients. Finally, several other projects aim to better understand patients' journeys, such as "NS-Park", which aims to model and improve the journey of patients with Parkinson's disease.

The American Entrepreneurship Model in Healthcare Sciences: What are the Best Practices?

During a roundtable discussion moderated by Pierre Courteille, Chief Commercial Officer and Vice President Business Development at Abivax and Vice President at France Biotech, experts from different backgrounds discussed American best practices for rapid growth of HealthTech companies.

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Pierre Courteille: The failure rate in the pharmaceutical industry is very high. Is this a handicap for European firms, where the notion of failure is less readily accepted than in the United States?

● **Marcello Starr.** Indeed, there is an idea in the United States that failure is common and understandable for entrepreneurs, and that they know how to deal with it. This is only partially true. Some of the investors I work with will not invest in a company if the executive has not faced a failure in recent years. Indeed, failure is a great way to learn, and an entrepreneur who has known only success is not necessarily aware of the factors that make him successful. Even from an investor's point of view, you have to accept the notion that all the companies in your portfolio may fail. Now, entrepreneurs are not always prepared to face failure. It is a very personal process and sometimes very difficult to handle. But there are ways to deal with it optimally, and this is in fact what I explain to my classes.

● **Jeffrey Hubbell.** Care is needed though: there are good and bad failures. If an entrepreneur fails to bring his team together around the project, to lead the research and development phases, or to develop a business strategy, it will be very difficult to get past such failure. On the other hand, if it comes from market risk, or if the technical or scientific hypothesis followed turned out to be incorrect, then it is more acceptable. But even in these cases, it is important to ensure that the necessary studies are carried out to limit risks.


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"The expectations of researchers in Europe concerning technology transfers are sometimes unrealistic."
Gil Beyen, Chairman and CEO of Erytech Pharma SA


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"The appeal of a place like Boston or San Francisco comes from its density of experts in the biotechnology industry."
Jeffrey Hubbell, Eugene Bell Professor in Tissue Engineering at the University of Chicago

Let's talk about efficiency in the HealthTech ecosystem. What makes the United States attractive today compared to Europe?

● **Jeffrey Hubbell.** The appeal of a place like Boston or San Francisco comes from its density of experts in the biotechnology industry. The number of scientists, investors and executives speeds up the work and facilitates meetings. It's a very special ecosystem. It is very simple to find the right people, despite the risk associated with companies. People know that if they fail, they will be able to bounce back easily with some other business without having to pull up sticks and move elsewhere with their families. The downside is that it is very difficult to hang onto talent. Typically, in Boston, your staff will receive a job offer every six months. So you have to be able to respond by raising wages on a regular basis.

● **Sophie Kornowski.** The ecosystem was born out of the excellence of great schools, such as Harvard Medical School and MIT. Many biotechnology companies now are spin-offs from these institutions. Next, the big pharma firms wanted to get closer to this innovation hub to be able to monitor young BioTechs and create partnerships.

"Many entrepreneurs drive their projects through vision and a desire to bring their innovation to patients. But they underestimate the amount of effort required."
Sophie Kornowski, Senior Partner at Gurnet Point Capital


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"Some of the investors I work with will not invest in a company if the executive has not faced a failure in recent years."
Starr Marcello, Deputy Head at Polsky Center for Entrepreneurship and Innovation; Assistant Professor of Entrepreneurship at the University of Chicago


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"Overall, American universities pay more attention to communication and presentation skills."
Melody Swartz, William B. Ogden Professor of Molecular Engineering at the University of Chicago


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The transfer of technology between universities and companies is not yet optimal in Europe, and in France in particular. What advice can you give to improve practices?

● **Gil Beyen.** There may be a lack of experience in this area in Europe as well as occasionally unrealistic expectations on the part of researchers. Indeed, when you look at the studies of royalty rates for licensing between Europe and the United States, you see that they are lower in the United States. The environment is more mature there and perhaps in Europe it is still difficult to transfer publicly funded research to companies.

How long does it take in the United States to transfer technology between a university and a company?

● **Jeffrey Hubbell.** Once the patent is filed, it takes only a few months to sign a license. Negotiations do not drag on. I agree with Gil; in my experience, expectations in Switzerland are a little too high and it is always a challenge to convince universities.

● **Sophie Kornowski.** It's hard to figure out whom to negotiate with in France. We are sometimes sent from one office to another. Although things have improved in recent years, there is still no sense of urgency. And sometimes it takes more than a year to get somewhere. Large pharma companies simply can't wait that long.

● **Jeffrey Hubbell.** I also sometimes wonder whether this difference in approach between the United States and Europe regarding technology transfer has something to do with the notion of failure. If the researchers' job is to get a deal, this encourages them to move quickly and on reasonable terms. But if the project is later successful and actually ends up as a drug, they may feel that not getting a better deal is in some way a failure.

● **Sophie Kornowski.** Technology Transfer offices need success. They may be excellent entrepreneurs, but we (the pharmaceutical industry) are still better equipped to negotiate, we have more time and we are better paid. So I think we also have to remain fair in these negotiations and give them and the universities an opportunity to sign equitable agreements so that no one will feel aggrieved if the drug actually makes it onto the market.

The issue of financing is still complex in Europe. What skills does an entrepreneur need to be able to present himself before investors?

● **Sophie Kornowski.** First, an entrepreneur must understand his business, his business plan and how much money he will need. Many entrepreneurs drive their projects through vision and a desire to bring their innovation to patients. But they underestimate the amount of effort required. Clinical trials, for example, often last 30-40% longer than the entrepreneur initially envisaged. So, of course, he must provide investors with a vision, science and passion, but also precise accounting figures. Then everything must be supported by evidence. The presentation is often very positive but is not always backed up by pertinent details. The entrepreneur must be totally transparent. Then you need a long-term goal, like putting the product on the market rather than simply seeking to make money through partnerships. It's important to work with people who want to see their company succeed.

Education systems in France and Europe are less entrepreneurial than in the United States.

● **Melody Swartz.** Overall, American universities pay more attention to communication and presentation skills. They may perhaps be too insistent in this regard, and we see the downside of that with the example of Elizabeth Holmes, who managed to deceive many people, including investors, with her company, Theranos. On the other hand, and I see this in Switzerland, I have many students from European countries who are much better at maths and science. But today, to get out of the engineering profession, become a manager and move up the ladder, it takes more than just an engineering background. You have to have the necessary confidence, and these skills should be taught a little more in Europe.

What other best practices make the difference today in the United States?

● **Jeffrey Hubbell.** Some U.S. universities, including Chicago, have set up a specific organization to help teachers turn more towards companies. They also offer tools to identify technologies that may be turned into a product.

● **Marcello Starr.** My advice is not to underestimate the quality of relationships. No entrepreneur can win without strong networks, not only with investors, but also with the talented individuals and people who can help the company move forward. We must not be afraid to invest in human relations.

● **Sophie Kornowski.** In addition, teams need to learn how to stay focused on their main goal. Sometimes a company loses its way because it wanted to move too fast towards other indications for its product, or because it signed too many partnerships, and so on. It is essential to stay focused and ask each time that something else is launched whether it is consistent with the core project. This is very important.

The "Bridging Academia with Industry" Model

Interviewed by Philippe Pouletty, co-founder and Managing Director of Truffle Capital, Gabriela Apiou, Director of Strategic Alliances at the Mass General Research Institute in Boston, details the translational research program designed to foster collaboration between hospital researchers and industry.

The number of patents proposed to industry by their inventor is very small. However, the expertise of the best academics serves as a tremendous lever for HealthTech. How can we bring them closer to the corporate world?

● **Gabriela Apiou.** Bridges must be encouraged in research, particularly at the international level. We want to treat cancer, Alzheimer's disease, and so on. These are very complex problems for all healthcare systems, and we need to work together to solve them and ensure that our science reaches patients. This is why we're extremely focused on this idea of bridging academia and industry. The Mass General is a hospital highly focused on innovation. It employs 8,500 people in the field of research, including 2,000 principal investigators (PI) across different therapeutic areas. Last year we published about 7,000 articles and obtained 200 new patents. And every year we participate in the creation of 20 to 30 start-ups. Thus, about 40% of our patents and portfolio projects go to companies, mostly start-ups, but also to larger drug companies. Some of them also go to other academic institutions.

What is the origin of this programe, Bridging Academia with Industry?

● A few years ago, we found that our research was not reaching its full potential. That's why a new strategy was launched, with the creation of the Research Institute, which is making its mark on all this work and ensuring its promotion. It's something very new. The program forms an integral part of the Institute and is based in the Office of the Scientific Director, who works at the hospital alongside researchers. I am leading this program today with my colleague, Pat Fortune, from the Innovation Office, our large tech transfer office, which oversees projects from development through to commercialization. Together, we work with researchers to improve their interactions with industry and their connections with Boston's extremely rich ecosystem.

"We found a few years ago that our research was not achieving its full potential. This is why a new strategy was launched with the creation of the Research Institute, which is really making its mark on our work."
Gabriela Apiou, Director of Strategic Alliances at the Mass General Research Institute in Boston

How are these projects developed?

● We always begin with the clinical observation of physicians and patient samples. The first step is to understand the problem that researchers have to solve. We then set up dedicated multidisciplinary teams. They use basic science, translational research, clinical care and biomarkers identified in samples to respond to medical needs, particularly in the fields of epigenetics, cancer immunology, neuroinflammation in neurodegeneration, rare diseases, cardiometabolics and the microbiome. To give you an example, on a microbiome study project concerning cardiometabolic diseases, we conducted a program that brought together nearly 120 PIs across 20 hospital departments. We first identified the questions addressed in each therapeutic field. Then we put in place a common research plan. This approach allows us to make sure we always incorporate biological understanding, technology and medicine in the solution we are building. This is a highly relevant approach in immuno-oncology, where the majority of patients do not respond to treatment. We must perform this multidisciplinary work to better understand what is going on.

What annual revenues are derived from these licenses or from collaborations with industry?

● Mass General's annual budget was about $900 million last year. This is a very significant amount, but we are now the largest hospital-based research enterprise in the United States. Approximately 40% of this sum comes from the National Institute of Health (NIH), 30% from private and public foundations, and 8% from royalties and licenses (approximately $72 million). The rest comes from internal mechanisms and philanthropy.


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