

The Health Valley: Global Entrepreneurial Dynamics

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Abstract: In the space of a decade, the Lake Geneva region has become the Health Valley, a world-class laboratory for discovering and developing healthcare of the future. Through visionary individuals and thanks to exceptional infrastructure this region has become one of the most dynamic in the field of innovation, including leading scientific research and exceptional actors for the commercialization of academic innovation to industrial applications that will improve the lives of patients and their families. Here follows the chronicle of a spectacular expansion into the Health Valley.

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The Health Valley is one of the fastest growing life science clusters in the world and has been rated the third European center for research into biotechnology and medical technologies after Cambridge and Oxford. It covers more than 750 biotech and medtech companies, 500 research laboratories, some 20 world-famous research institutions, universities and university hospitals, as well as numerous bodies supporting innovation, including science parks, incubators of start-up companies and venture capital funds. Above all, it is a center of excellence that attracts many famous scientists. This stems as much from its dynamic nature as from its resources in research and development and its dense industrial fabric, which offer so many opportunities.

Today, on account of its excellence and supportive environment, the Health Valley is a premier location for industries active in the life sciences. The proof lies in the many companies working in medtech and biotech which have established themselves in the region, including Baxter, Beckman Coulter, Celgene, Debiopharm, Edwards, Ferring, Johnson & Johnson, Lonza, Merck Serono, Medtronic, Stryker, and UCB Farchim and, more recently Alcon, Alexion, Ariad, Nestlé Health Science, just to mention a few. Even better, tomor-

row's companies are already here. For example AC-Immune, Biocartis, GeKyoTex, Novimmune and many others are all growing companies whose roots are fed by the innovations originating from our research institutions and who benefit from our supporting environment.

Anticipate the Challenges of Tomorrow

We are at a turning point in the history of medicine. The confluence of innovations in computing, engineering and biotechnology will revolutionize medicine. It is therefore not surprising that our politicians, payers, the pharmaceutical industry and patients observe us and expect us to deliver better solutions to health problems. The goals are to ensure that medicine meets the needs of an aging population, that it can be financed and is capable of responding to the new needs that are upon us, which include chronic diseases (estimated to be 80% of the total health budget in 2030). Diabetes, atherosclerosis, Alzheimer's, Parkinson's are just a few examples of endemic diseases. The demographic challenge: we live longer. In less than 50 years, we have gained 10 years of life expectancy. But far from being satisfied with simply adding years to life, we need to enable a high quality of life during those additional years. And this trend can be enumerated. Already, in the space of 15 years, we have increased our quality of life by 15%, if one looks at the percentage of healthy people between the ages of 65 and 74. Another challenge is the financial burden of aging. Starting from the age of 60, health care costs increase by more than 50% with every 10 years of life.

Our Recipe: Integration and Openness

It has been said that a single cell contains an entire universe. In the Health Valley region, life itself – from the molecular to the industrial – is a vast landscape of excellence in both the academic pursuit of knowledge and entrepreneurship. In short, the Health Valley is a fertile cluster of opportunity that has managed to create an enviable position. In this process, openness and integration have played essential roles.

Promoting the Free Circulation of Ideas

During the 16th century, leading scholars – such as Paracelsus, Andreas Vesalius and Erasmus of Rotterdam – came to Switzerland to have their theses or essays printed, making the region an integral part of the Renaissance humanist movement and its scientific progress. Closer to our time, one of our keys to success has been our capacity for innovation. Indeed, our higher education institutes attract first-class talent – both from Switzerland and abroad – in a globalized environment. Such openness is a valuable asset that can be measured by, among other things, Switzerland's degree of international competitiveness in the field of knowledge.

Integration and Valorization of Know-how

The expansion of our industry has been driven by generations of entrepreneurs who settled inside the Swiss borders. Among the most significant contributors were the Huguenots, who introduced us to the worlds of chemistry and watchmaking. Having fled France after the revocation of the Edict of Nantes in 1685, weavers and

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BioAlps

BioAlps represents and facilitates the life science cluster of Western Switzerland and notably biotechnology and medical technology. Dedicated to promoting excellence and innovation in the sector, BioAlps is known as Europe's leading bio-cluster for the life science industries and is playing a critical role in supporting Western Europe's biomedical innovation.

Formed as a non-profit association, BioAlps is composed of cantonal members and academic and research institutions in Western Switzerland. It is supported by the Cantons of Bern, Fribourg, Vaud, Neuchatel, Geneva, Valais, Jura and the Swiss State Secretariat for Economic Affairs (SECO).

BioAlps aim is to promote Western Switzerland as a world class center for the life sciences, and to foster the growth of this specific industrial sector. Its role goes well beyond the promotion of excellence in the sector as it exists today. BioAlps also accompanies, supports, encourages and stimulates both performance and innovation by creating the conditions that enable the development of companies. It pursues an aggressive technology agenda in the region at all levels: regionally, nationally and in the international arena. BioAlps also promotes synergies between academia, entrepreneurs, investors, authorities and new businesses to translate ideas into new products and bring new technologies to market.

silk merchants turned Basel into the ribbon capital of Europe. The need for dyes encouraged the chemical industry to take root, leading later to diversification into fine chemicals and, finally, into pharmaceuticals. The history of watchmaking followed a similar arc, building on skillful craftsmen who brought to Switzerland not only their watchmaking know-how but also the capital needed for the development of a hi-tech industry – capital that continues to irrigate our fertile country.

Supporting Entrepreneurship

Behind every great innovation there are human beings. Here, too, there are many examples of integration: Nestlé was founded by a chemist of German extraction, Henri Nestlé; Xavier Givaudan was French; and Charles Eugene Lancelot Brown, who had dual Swiss–British nationality, founded Brown, Boveri & Cie with the German-born Walter Boveri. On a more contemporary note, pharmaceutical industrialists such as the Bertarelli and Mauvernay families settled in our country to create and develop their own businesses... and with the Blue Brain project and the establishment of Campus Biotech in Geneva and soon the Agora cancer center in Lausanne the story continues, constantly adding entrepreneurial dynamism to the Health Valley.

Capitalizing on Interdisciplinarity

As early as 1761, in the introduction of his famous Encyclopedia, Denis Diderot wrote: "There are two ways of developing Science: one is to increase the mass of knowledge through discoveries; the other is to bring discoveries together, and organize them..." Bringing the mass of knowledge together is what began in the 18th

century, and has become a necessity in the 21st. Take the life sciences, for example. One of the hallmarks of our region is that it can count on skills that go way beyond biology and medicine. Our expertise in micro- and nanotechnologies as well as in chemistry, computer science and even communication and finance are essential both to integrate knowledge gained by the different disciplines and to develop novel therapeutic approaches. In summary, we count among us both the innovators as well as the intermediaries who organize and disseminate innovation for mankind's benefit.

Creating a Culture of Innovation

The innovation process needs more than the classic environment that builds on

an organization's internal resources (*e.g.* idea management systems for its collaborators and internal incubators to valorize its R&D). Rather, such processes must organically develop in parallel, reacting to the fact that the boundary between an organization and its ecosystem tends to blur. The trend is towards openness – or open innovation – a process that consists of going to fetch the knowledge or even the resources outside individual highly focused organizations and, *via* collaborations which provide resources, cross-disciplinary knowledge and competencies to the ecosystem. Companies, universities and technology transfer organizations have all developed participatory ways of transferring knowledge. UniverCité, based in Renens, for instance, following the global DIYbio trend, is positioning itself at the interface between industrial design and life sciences. It is offering almost 1000 square meters of open lab space and is open to the public at large. Campus Biotech enables neuro-engineering and advance medical care. Agora will improve cancer care and catalyze development of better treatments for cancer.

Without this ecosystem, featuring a highly interconnected environment, neither the Health Valley nor any of its industrial, academic or entrepreneurial actors could imagine staying at the cutting edge of patient care and innovation. Nor do they believe that they are the sole bearers of knowledge. Knowledge can be found everywhere; collaboration and exchange enrich it continuously. Our region understood this long ago and has developed a tradition of advocating integration and openness. This is the spirit that nurtures all the actors of our community.

The Wyss Center for Bio- and Neuroengineering

The Wyss Center for Bio- and Neuroengineering is a newly established research center that aims to create innovative neurotechnology for human benefit. The Center aims to accelerate the translation of scientific, clinical and engineering innovations into real world products. It focuses on neuroscience advances that will prevent, diagnose or treat nervous system disorders, or lead to useful neurotechnologies. The Center drives innovation and development by providing a set of highly integrated science, engineering, clinical, and product development related platforms coupled with specific project funding programs. The Center platforms facilitate design, development and implementation of new technology. Working as partners, the platform teams advance high impact, high risk projects from concept to a level where they are attractive for early stage investment and commercialization. The Center fosters academic, clinical and industry collaborations related to neuroscience and neuroengineering that range from early concept, to preclinical validation, to critical proof of concept clinical trials and on to realization as a useful product. The Center was established by a gift from Hansjörg Wyss and by the Ecole Polytechnique Fédérale de Lausanne (EPFL) and the University of Geneva (UNIGE). The Wyss Center is housed in the new Campus Biotech campus in Geneva whose infrastructure is organized and supported by Foundation Campus Biotech Geneva, which is a joint initiative of the EPFL, the state of Geneva and the UNIGE.

THE GREAT STAGES OF THE ADVENT OF THE HEALTH VALLEY

First French speaking Swiss biotech to be publicly traded; Modex launches a takeover bid for its rival IsoTis - Creation of Addex Pharmaceuticals in Geneva - Launch of Ecllosion (see box), the lemanic life sciences incubator – Launch of the School of Life Sciences at EPFL.

The UNIL inaugurates its integrative genomics center, contribution of the upper school in Lausanne to the SVS program - First resounding failure in the field of biotech companies: GeneProt ceases all activity.

The German group Merck KGaA buys Serono and gives birth to Merck Serono, which markets drugs particularly in the areas of oncology, neurology and fertility.

The announcement of the closure of Sécheron by the pharmaceutical company Merck Serono, in April 2012, left this beautiful complex without occupants or functions... until a consortium formed by Hansjörg Wyss and the eponymous foundation, the Bertarelli family, the University of Geneva and EPFL decided to revive it a year later, with a wild bet to invest the larger part of some 40,000 square meters available to develop a new cluster dedicated to neuro-and bioengineering. Campus Biotech was born. By the excellence in research that will be conducted there, access to high-performance platforms, the promotion of synergies and the sharing of the same ambitions, Campus Biotech creates for itself the means to have a campus whose impact will be world class.

Celgene invests in a second production site in Neuchâtel - Entitled UniverCité, the first community laboratory in the field of Life Sciences opens in Renens / Vaud: the goal is to empower individuals outside of academic or institutional structures while facilitating their access to the scientific establishment, by sharing infrastructure and knowledge in order to democratizing the tools for innovation. Until now, biology had remained an orphan of this « hacker » revolution that had already conquered the computer and many other hard sciences: 1,000 m² available to the whole community because innovation comes from unexpected sources - CSL Behring decides for Lengnau (BE) as the location for a new production plant.

2001

On July 3, the Universities of Lausanne (UNIL) and Geneva (University of Geneva) and the EPFL decided to collaborate and signed the agreement Sciences-Life-Society (SVS) - Foundation of BioAlps: the cluster of life sciences in Western Switzerland was born.

2002

2004

The University of Geneva, UNIL and EPFL launch a new platform, the DNA Array Facility (DAF), dedicated to the analysis of genes expression and the CIBM (Center for Biomedical Imaging).

2005

2006

AC Immune sign an agreement with Genentech for a potential value of \$ 300 million - Ferring settled its global headquarters in Saint-Prex.

2007

2008

Full integration of the Swiss Institute for Experimental Cancer on Research (ISREC) into EPFL - Launch of the Centre of neuroprostheses with the support of the Bertarelli Foundation, Defitech and Sandoz.

2009

The Geneva start-up NovImmune raises a record \$ 62.5 million francs to finance its clinical development.

2010

Nestlé announces the creation of the Nestlé Institute of Health Sciences in the Innovation Park at EPFL - The Ludwig Institute integrates the Lausanne branch of the Institution at UNIL - UCB to invest CHF 300 million in a new production unit in Bulle/Fribourg.

2011

BioAlps, the cluster of Life Sciences of Western Switzerland celebrates its 10th anniversary and with it, 25,000 professionals of Life Sciences, 19 upper schools and close to 750 companies – Publication of "Health Valley", the biotech thriller on the edge of reality, to establish the "Health Valley" brand in the life sciences community.

2012

2013

The EU decides to support the Human Brain Project: a billion euros project over ten years. This flagship project of the Ecole Polytechnique Federale de Lausanne (EPFL) aims to simulate the human brain using computers, an historical decision that makes Health Valley the European Capital of neuroscience Pioneer in bioinformatics, the Swiss Institute of Bioinformatics (SIB) developed the algorithm for the first non-invasive test to diagnose Down syndrome, with more than 99% fidelity.

2014

Ecllosion

Ecllosion's state-funded incubator has the mission to help researchers transform high-level science developed in the labs into a commercial project, with the proof of principle for the intended applications and a plan to develop them; at which stage the start-up can be launched and supported by private equity investors. The objective is to accomplish this 'translation' from lab to first round of VC funding in 18–24 months.

The Geneva region is an international center of excellence for life sciences research, and a domain where one can directly convert knowledge into economic value and jobs. Key success factors are the quality of the innovations and know-how developed as well as the excellence of management and workforce; not the size of the local market or the cost of the unskilled labor. Ecllosion offers specialized knowledge both from the business and life sciences point of view, and an advisory board covering all the different areas from regulatory to commercialization. Its high value-added labs offer the complete infrastructure needed for early development and it is deeply rooted into the region's academic and industrial networks to access to specific knowledge, services and infrastructures as required. After 10 years of operations, Ecllosion has served as a launch platform for 16 high potential start-ups, including for example GenKyoTex and GeNeuro.

Bioconvergence as a Driver of Change

Our interdisciplinary approach is our greatest asset, whereby biology and medicine can take full advantage of advances in other technologies, like computing and engineering. Barely visible to the general public, yet a true engine of change, technological advances are constantly opening new avenues to support the revolution in the medical world.

Apart from its capacity for fundamental research, our region has the technological means to advance the different disciplines that sustain this convergence and support the revolution of medicine which is becoming increasingly predictive, preventive, personalized and participatory.

The concept of 'one pill for all' is rapidly becoming the 'old' approach to medicine. Little by little researchers discover the different families of pathologies linked to a disease and, for each family, the precise molecular mechanisms that cause disease. It will be possible, based on new molecular sciences, to identify specific therapeutic targets and to test medicines that engage them using equally innovative biological models designed to help us understand disease and test tomorrow's medicines. This new knowledge also will allow design of new diagnostics based on these molecular markers at the same time.

Based on the identification of predispositions, preventive medicine will emerge, to help modify the behaviors of individuals with regard to their health and, in some cases, begin preventive treatments.

Thus we move from classical western medicine that relies heavily on anamnesis – (medication) and hospitalization to

a practice that integrates prevention, diagnosis and personalized treatment into new approaches that are the result of a new way to conduct medical research: transdisciplinary, translational, using all the advantages of scientific and technological progress. Finally, the participatory dimension of medicine is facilitated as patients will be empowered by technology to become more active participants in their own care. Indeed, if medicine has always been a matter of data (symptoms, temperature, pulse, test results, etc.), today these data have become digital, even as they multiply exponentially they become more manageable and circulate with fewer limitations under the control of patients and authorized medical and research professionals. This opens new horizons for researchers and transforms their relationships with patients.

A Region in Perpetual Edification

The Health Valley has all the ingredients needed to be a major player in the medical revolution: hospitals, universities, technical schools, technology institutes, entrepreneurs and even experienced specialized investors. In addition it also demonstrates ambition and courage in both research efforts and in creating an ecosystem that facilitates the emergence of industrial players of tomorrow here

ASSEMBLING PROJECTS

The academic and industrial worlds have gone from a silo model to that of an open source operations network that showcases the joint research projects, public-private partnerships and major research infrastructures.

Already in 2000, the Lake Geneva Region was negotiating a turning point with the project "Life-Science-Society" (SVS). Spurred on by their respective managements, EPFL, the UNIGE and UNIL proceed to an extensive redistribution of cards aimed at bringing together teaching and research of certain disciplines to avoid duplication and achieve a critical mass. The UNIL abandons chemistry, physics and mathematics which were taken over by EPFL, and Geneva was awarded the pharmaceutical sciences. This restructuring is the prelude to several groups and joint projects, which will, in future years, combine under major themes, such as the concentration of Cancer Research in Lausanne at Agora or the ongoing formation of a global center for neuroscience at Campus Biotech in Geneva. These are opportunities not only to redistribute tasks at different locations based on the skills of each region, but also to strengthen and crystallize a common vision to promote stronger horizontal structures, rather than competing vertical ones, thus allowing regional groups to compete internationally instead of regionally.

Campus Biotech (Geneva)

With the support of the Bertarelli family and the Wyss Foundation, the EPFL and the University of Geneva are in the process of transforming the former headquarters of Merck Serono into a new center of excellence dedicated to neuro- and bioengineering. Eventually, nearly 1,000 researchers, entrepreneurs and industrialists will occupy the campus, promoting a translational and interdisciplinary approach.

Commissioned in **2014**
Staff: > **1,000**
Cost of the project > **300 Mio**
Area: **40,000 m²**

The Wyss Center for Bio & Neuroengineering (WCBN) (Geneva)

Made possible by a donation from philanthropist Hansjörg Wyss, the WCBN can be considered as a focal point and "translational engine" of the Biotech Campus. The main mission of WCBN is to facilitate and accelerate the development of technologies and products applying synergies between research groups and industrial skills. This approach will lead to clinical applications that can then be translated into products on the market, for the benefit of patients.

Commissioned in **mid 2014**
Staff: **300**, the majority remain **dependent on their institutions**.
Cost of the project: **100 million over 6 years (operating costs)**
Area: **hosted by Campus Biotech**

BATLab (Geneva)

BATLab is the new building for laboratories of HUG and will be operational in late 2014. At inauguration, 32 laboratories and about 350 specialized employees will move into the new building. Serving both employees and patients, the BATLab project

meets the requirements of medicine of an evolutionary laboratory that is becoming increasingly important, leading hospitals to face new challenges.

Commissioned **end 2014**
Staff: > **350**
Cost of project > **65 Mio**
Area: **13,000 m²**

GENÈVE [GE]

HEALTH VALLEY

www.healthvalley.ch

DELÉMONT [JU]

Microcity (Neuchâtel)

Microcity lies at the heart of what is expected to become in time one of the largest centers of Microengineering expertise in Europe. Once completed, it should have 12 chairs and a staff of approximately 300 employees. In addition to EPFL, it houses the Neuchâtel Science Park NEODE, an incubator of start-ups. The geographical proximity of the new building to other organizations such as the CSEM and HE-Arc allows strengthening synergies,

for example in the sharing and use of certain equipment as a function of the needs of researchers. The proximity of Neuchâtel economic promotional activities is also an asset in the development of relations with industry.

Commissioned in **2013**
Staff: > **600**
Cost of project > **70 Mio**
Area: **10,000 m²**

UniverCité (Vaud)

Based in Renens, UniverCité is an open space which militates in favor of democratized research where it will be possible to develop breakthrough technologies at the crossroads of various disciplines, such as medical and design technologies, while still serving the public, the primary beneficiary of these technologies.

UniverCité is part of the global movement of participatory science "DoItYourself biology" or "DYIBio" born in the United States in 2008. This growing movement brings together more than 5,000 people around some forty community laboratories such as Genspace in New York, Biocurious in California, Madlab in Manchester, England, or La Paillasse in Paris.

Commissioned in **September 2014**
Staff: **Laboratory Community (100)**
Cost of project: **voluntary work**
Area: **1,000 m²**

NEUCHÂTEL [NE]

BERNE [BE]

FRIBOURG [FR]

LAUSANNE [VD]

Agora (Vaud)

Located on the site of the CHUV, the future AGORA Cancer Centre will be the core of the new Swiss Cancer Centre of Lausanne whose governance will be carried out jointly by the CHUV, UNIL, EPFL and the ISREC Foundation. Through the creation of this gigantic "toolbox" against cancer, this center will allow everyone to tap into the reservoir of available means with the aim of overcoming the diseases:

innovative advances in the knowledge of specific disease mechanisms, optimized administration of targeted therapies, and network implementation of the progress in the service of patients undergoing treatment.

Commissioned in **2016**
Staff: > **400**
Cost of project > **70 Mio**
Area: **11,500 m²**

Extension of CMU (Geneva)

The completion of the CMU meets the needs of the University of Geneva in the field of Life Sciences, one of its areas of excellence. The new building will include in particular the School of Pharmacy of Geneva-Lausanne (EPGL), the Section of Dental Medicine (SMD) research laboratories in clinical investigation (INVESCLIN), the Geneva Tumour Registry (GTA) or even the Unit of Development and Research in Medical Education (UDREM).

Commissioning in **2015-2016**
Staff: > **1,000**
Cost of project > **149 Mio**
Area: **21,000 m²**

SION [VS]

EPFL VALAIS-WALLIS Campus (Valais)

Based in Sion on the site previously occupied by Espace Création, it will bring together 11 chairs, two of which will be dedicated to neuroscience and two others to biotechnology.

Commissioned **beginning of 2015**
Staff: > **300**
Cost of the project **115 Mio**
Area: **15,000 m²**

in the Health Valley. This ensures that the most promising intellectual property also creates jobs and wealth locally instead of simply migrating to Silicon Valley.

Among the most significant and ambitious projects are: in Geneva, the extension of the CMU (Academic Medical Centre), the laboratory building of HUG, Campus Biotech, the Wyss Center (see box); and in Lausanne, the ISREC/AGORA, a new international cancer center featuring translational research that will quickly move concepts developed in the laboratory to therapeutic improvements at the bedside, and, of course the EPFL, which embraced the life sciences and became a major player in this field, reaping the laurels of the European programs, including the FET Flagship Human Brain Project which will be conducted with a one billion euros budget. But the major accomplishments do not stop there. For example, the Microcity in Neuchatel and EPFL Valais at Sion have extended regional excellence and competencies, leveraging synergies with local actors and opening a more ambitious potential.

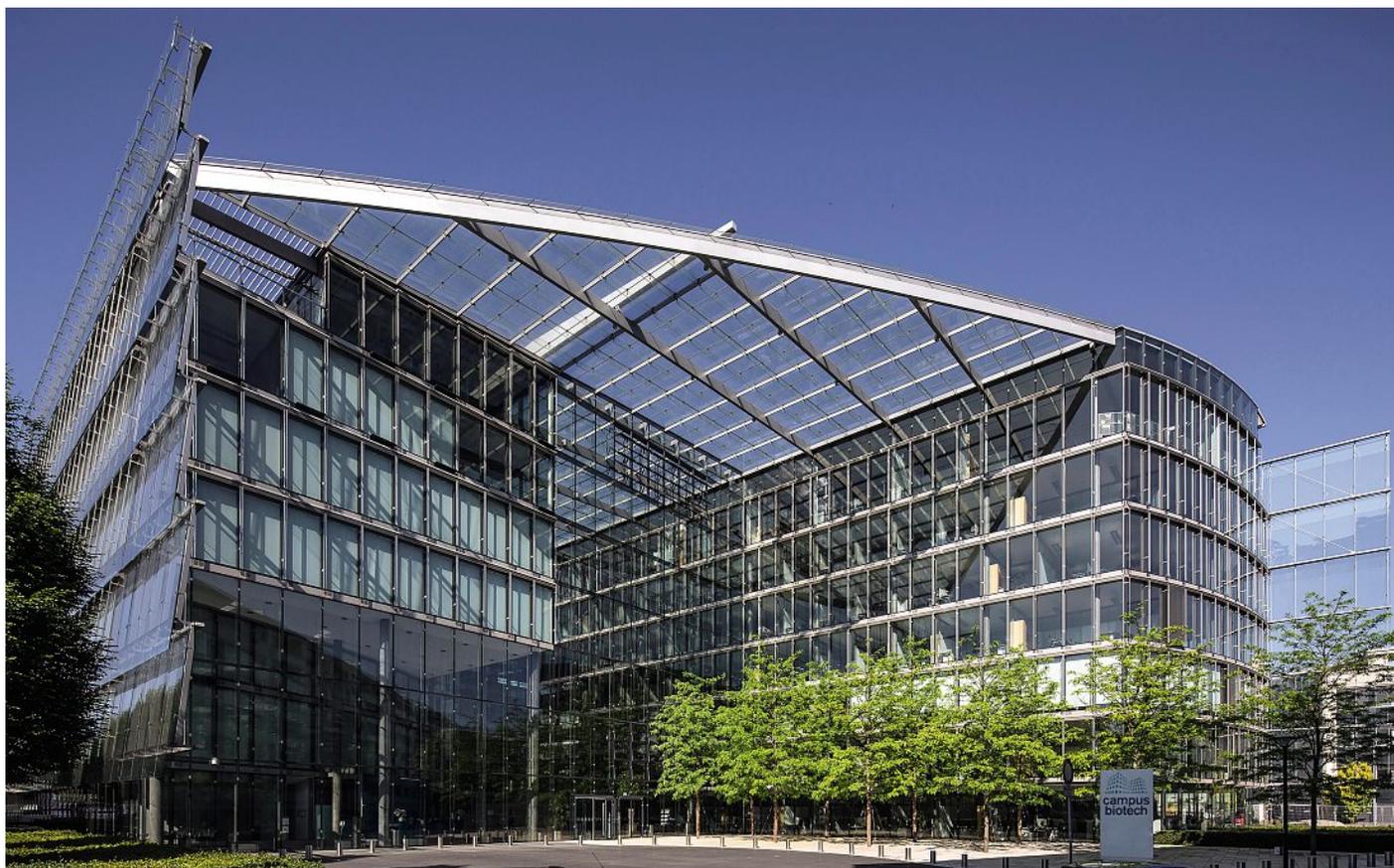
Translate Innovation in Solutions and Products

But beyond the scientific and technological innovations of Health Valley, it is critical to ensure that these discoveries shall be translated into measurable benefits in the clinic and that they will be put to the service of the patient as soon as possible. There is always a long maturation time between scientific discovery and clinical application. Pasteur and Koch highlighted the existence of germs in the 19th century. It took a generation to benefit from the contribution of antibiotics. The aim should be to continue to reduce this time to a minimum; and, for that, it is necessary to test these new approaches and new active substances as efficiently as possible in order to answer a simple question: do they help save lives, improve quality of life? To do this we need to empower competent intermediaries (*i.e.* entrepreneurs and investors) and provide an environment that will encourage them to create jobs and local wealth here, in Health Valley.

Global Entrepreneurial Dynamics

In short, the Health Valley is abundant with opportunities. It has allowed a number of companies, for example AC Immune, Shire, Merck Serono, Ariad, Alexion to experience exceptional growth, justifying the several hundred millions invested over the past few years by companies such as UCB, Celgene and CSL. Its assets are the basis of the success of companies including Ferring, J&J, Medtronic, Debiopharm, Nestlé Health Science and many others. Whether we look at regional competitiveness on the level of investment, the demand perspective, products, technologies, the financial situation of industrial companies, the technological quality, the level of training/competencies, entrepreneurial drive; all of the indicators are positive for the region to be competitive on a global scale. Our ambition is to make sure that our region maintains its leadership in innovation and guarantees its prosperity in an increasingly competitive and fast-paced world. We are doing this by focusing on the fundamentals, creating an optimal environment for the exceptional people who are the cornerstone of our academic, industrial and entrepreneurial community.

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Campus Biotech is a new centre of excellence in biotechnology and life science research. It focuses on science and its translation into products that have an impact on society and the world. Campus Biotech is expected to generate a vast range of opportunities, bringing impetus and investment to this vital economic and scientific sector. The building that has housed the former Merck Serono headquarters, and which is now home to Campus Biotech, was conceived as not only a hub for science and research, but also a place for people to meet and a place to be enjoyed.