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We invest in technologies that we believe will shape the future, and we see them realised through instruments that support both fundamental discovery and real-world application.

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As global science faces mounting complexity, the Paul Scherrer Institute (PSI) stands out as a model of long-term vision, technical excellence, and interdisciplinary ambition. Director Christian Rüegg discusses how PSI is advancing the frontiers of oncology, neuroscience, energy, and AI - developing radiopharmaceuticals and imaging entire neural networks, to enabling dynamic drug interaction visualisation and pioneering synthetic fuel research.

How does your scientific background align with the mission of the Paul Scherrer Institute, and what role does the institute play in Switzerland and beyond?

My academic foundation is in condensed matter physics, having studied at ETH Zurich and completed part of my doctoral research at the Paul Scherrer Institute (PSI). Although I am not a biologist and do not work directly in the pharmaceutical sciences, I have always been fascinated by the interface between fundamental research and the development of advanced scientific infrastructure, particularly large-scale instruments that enable high-precision investigations. This focus aligns closely with PSI's mission, which is rooted in creating and operating such infrastructure to support a wide range of disciplines, including pharmaceutical and life sciences research.

PSI is the largest research institute for natural sciences and engineering in Switzerland. It is the central location of Switzerland's large research facilities and part of the ETH Domain. Our mandate is to conduct mission-oriented research, foster technological development, and build and operate

large-scale facilities that are beyond the reach of individual institutions or even most private-sector actors. Among these are the Swiss Light Source, a synchrotron, and the Swiss X-ray Free Electron Laser – a facility spanning approximately 740 metres in length – both indispensable tools for advanced imaging and structural biology.

While these facilities are funded at the national level, they are fully open to international collaboration, welcoming both academic and industrial researchers. Located just 30 kilometres from Zurich and Basel, and close to Zug, PSI is embedded in the heart of Switzerland's pharmaceutical corridor, positioning the institute as a globally connected hub for scientific innovation and interdisciplinary research.

How is Switzerland's national research landscape structured with regard to health innovation, and what distinctive role does PSI play within this framework?

Switzerland's research landscape is notably decentralised compared to countries with centralised institutions such as the National Institutes of Health (NIH) in the US, which oversees an array of specialised centres dedicated exclusively to health. The Swiss system comprises four national laboratories within the ETH Domain, with the PSI standing as the largest. PSI is a key driver of health innovation, although its remit extends well beyond the biomedical sphere and includes areas such as fundamentals of nature, future technologies, energy and climate science. Its work is complemented by institutions like the Swiss Federal Laboratories for Materials Science and Technology which specialises in materials science, including research on biomedical implants, and by two additional national institutes that address environmental health.

Alongside these research centres, health-related science thrives within Switzerland's leading academic institutions, such as ETH Zurich, the Swiss Federal Institute of Technology Lausanne (EPFL), and the various medical universities, even though PSI itself does not have a medical faculty. This distributed, interdisciplinary approach allows Switzerland to advance health innovation through a combination of infrastructure, applied research, and collaboration, positioning PSI at the heart of a broad ecosystem that spans materials science, environmental studies, and the life sciences.

What is the IMPACT project, and how does it reflect the Paul Scherrer Institute's contribution to innovation in cancer diagnosis and therapy?

PSI is leveraging its deep expertise in accelerator science and radiochemistry to advance health innovation, most notably through the IMPACT project – Isotope and Muon Production using Advanced Cyclotron and Target technologies. The Isotope production part of this ambitious upgrade to PSI’s world-class proton accelerator aims to enable the generation of new isotopes with interesting properties for medical applications, in particular for theranostics, where different isotopes of the same chemical element are used for diagnostic imaging and targeted radiotherapy. These isotopes can be attached to molecules specifically targeting target cells. In theranostics they first localise tumours via PET-CT imaging using an isotope which is suitable for imaging. The same marker with a different isotope from the same chemical element is then used to deliver radiation with therapeutic potential – such as alpha particles – to selectively destroy cancer cells. The ability to produce different isotopes from one element with this dual functionality marks a significant step forward in precision oncology.

This initiative builds on PSI’s long-standing contributions to applied cancer care, notably its in-house development of proton therapy, which treats approximately 350 patients each year with exceptional precision. It mainly draws on the work of the Centre for Radiopharmaceutical Sciences, a joint applied research lab between PSI and ETH Zurich. It has leading bench to bedside research capabilities in radiopharmacy in Switzerland including cutting-edge knowhow in isotope production, GMP-grade pharmaceutical development, and clinical collaborations, such as ongoing studies with the University Hospital Basel.

Through IMPACT, PSI will dedicate a portion of its high-energy beamline to medical isotope production, establishing a new facility designed to support both internal research and broader clinical applications. The project brings together five of PSI’s Centers, including the Center for Accelerator Science and Engineering, the Center for Life Sciences and the Center for Nuclear Engineering and Sciences.. The facility will take several years to complete and is an integral part of the Swiss Roadmap for Research Infrastructures. It stands as a flagship of PSI’s health innovation agenda, demonstrating how technological and research excellence can be harnessed to drive meaningful progress in cancer diagnostics and treatment.

How does PSI’s multidisciplinary environment foster innovation, and what are the advantages of having all expertise concentrated on a single campus?

The institute’s ability to unite a broad range of scientific disciplines within one integrated campus is both a logistical challenge and a unique strategic advantage. While managing collaboration across

fields as diverse as life sciences, radiochemistry, and accelerator physics requires bridging distinct research cultures, the outcome is a fertile ground for innovation. What sets PSI apart is not only the sophisticated technologies it develops but also its proven ability to orchestrate large-scale, technically complex projects involving diverse expert teams. This coordination is supported by a strong project management culture and a shared commitment to tackling ambitious scientific goals.

Having all divisions in close physical proximity allows for seamless interaction, spontaneous consultation, and real-time collaboration, conditions that are difficult to replicate across dispersed sites. This spatial integration encourages a deeply collaborative spirit where problems are approached collectively and solutions emerge from cross-disciplinary insight. Personally, I find it particularly rewarding to work in an environment where fundamental scientific questions are addressed through the creative application of advanced technologies. PSI's model demonstrates that when the right expertise is brought together under one roof, complexity becomes not an obstacle, but a catalyst for transformative science.

How does PSI support the translation of research into commercial ventures, and what does the success of Araris Biotech illustrate about this model?

PSI engages extensively with industry across multiple fronts, from collaborative research and facility access to technology licensing and company creation. One of the most established pathways is the use of PSI's synchrotron for structural biology, with pharmaceutical companies leveraging its beamlines to analyse proteins at atomic resolution, contributing to more than 10,000 of the 150,000 protein structures currently known. Underpinning these capabilities are innovations like those developed by LeadXPro, a PSI spin-off which now offers gene-to-structure services to major pharmaceutical companies worldwide. It uses its expertise in developing its own proprietary structure-based targets and leads..

To further accelerate impact, PSI actively encourages entrepreneurial thinking within its scientific community. Since 2017, the PSI Founder Fellowship has provided structured support for early-career researchers interested in commercialising their ideas. Selected through a competitive process, fellows receive up to 18 months of funding and institutional backing to refine their concepts and develop viable ventures. The programme, supported in part by UBS (Union Bank of Switzerland), has funded around 15 individuals to date, with over half going on to found companies. Araris Biotech, launched 2019 following a 2017 fellowship, stands as the programme's

flagship success. Originating from an initial CHF 150,000 investment, it has since grown into a biotech enterprise valued at USD 1.14 billion, a striking example of PSI's capacity to translate deep science into global commercial outcomes.

While many PSI spin-offs emerge from highly specialised technological domains such as detectors, accelerators, and materials science, and tend to grow through innovation rather than rapid scaling, the Araris story demonstrates that with the right combination of scientific excellence, institutional support, and early-stage funding, even deep-tech ventures can achieve transformative scale in the biopharmaceutical arena.

How would you evaluate the strengths and limitations of Switzerland's entrepreneurial environment for science-based start-ups?

While Switzerland is best known for its global corporate powerhouses in finance, pharmaceuticals, and commodity trading, it also possesses a quietly robust entrepreneurial fabric, anchored by a dynamic network of SMEs. Operating within a high-wage economy, Swiss SMEs are under constant pressure to innovate, producing high-value, technologically advanced goods, an expectation that has become ingrained in the industrial mindset. This culture of innovation is strongly supported by institutions such as ETH Zurich and EPFL, both of which have become fertile ground for spin-offs in recent years, particularly in emerging fields like artificial intelligence. ETH Zurich alone now produces around 40 start-ups annually.

Despite these strengths, access to scale-up capital remains an ongoing challenge. Early-stage support is increasingly available, yet direct investment from private individuals into high-tech start-ups is still uncommon, prompting many companies to look abroad for growth financing or public offerings. While some may view this international focus as a structural weakness, in reality, it reflects a pragmatic understanding of the country's size and market limitations. Switzerland must embrace the reality that ambitious ventures cannot remain confined to a domestic base.

The case of Araris Biotech is illustrative. Although a local acquisition by a Swiss pharmaceutical leader may have been feasible, the company ultimately found the right strategic fit in Japan. In most instances, particularly beyond life sciences, companies must naturally look to Germany, the United States, or other markets to realise their full potential. In this context, Switzerland's strength lies not only in its capacity to generate world-class innovation, but in its ability to prepare that innovation for global relevance.

How does PSI collaborate with industry, and in what ways could these partnerships be further strengthened?

For over two decades, PSI has maintained close, pragmatic relationships with industry through a model in which public investment in world-class research infrastructure enables companies to access sophisticated instruments to solve targeted R&D challenges. This dynamic is especially evident in structural biology, where pharmaceutical firms have long relied on PSI's synchrotron facilities to analyse protein structures essential for drug discovery. It forms part of a broader, well-functioning innovation ecosystem, where institutions like ETH Zurich and EPFL educate top-tier scientific talent, and PSI provides the advanced capabilities required to translate that expertise into tangible innovation.

While this access-based model has delivered significant value, PSI sees untapped potential in evolving these relationships towards deeper, more collaborative partnerships. Industrial stakeholders are often reluctant to invest in long-term instrument development, preferring to engage only once technologies are fully operational. However, early-stage co-development could foster more strategic alignment, in terms of both design input and financial participation. Beyond transactional interactions, PSI advocates for new formats of co-innovation that encourage shared problem-solving from the outset.

One of these strategies is Park Innovaare, a new innovation park of Switzerland Innovation, connected directly to PSI. This direct connection provides an excellent opportunity for intense collaboration with industry. Park Innovaare focuses on the innovation priorities of accelerator technologies, advanced materials & processes, human health, and energy. It offers a network and environment in which companies, SMEs, startups and PSI can collaborate optimally to drive forward and bring innovative products and processes to market.

What is the objective of PSI's participation in the NIH brain mapping project BRAIN CONNECTS, and how could this effort transform neuroscience research?

PSI's involvement in the NIH brain mapping project BRAIN CONNECTS represents a notable instance of United States federal funding supporting scientific research beyond its borders, an exceptional endorsement of PSI's technological capabilities. The initiative is led by Dr Adrian Wanner, a neuroscientist formerly based in the US, who relocated to Switzerland to leverage PSI's newly

upgraded synchrotron. This outstanding facility delivers imaging precision several orders of magnitude beyond standard medical CT scans, enabling researchers to visualise biological structures at nanometre resolution. Building on prior work in vascular imaging, this next phase aims to chart the brain's connectivity at the synaptic level – an undertaking with transformative implications for the study of neurodegenerative diseases and brain function more broadly.

At the heart of this project lies a convergence of advanced instrumentation, algorithmic computation, and interdisciplinary collaboration. The ambition is to move from detailed imaging of vascular systems to full-scale neural circuit mapping, generating data-rich reconstructions that could fundamentally shift our understanding of how the brain is wired. This approach combines ultra-high-resolution imaging with powerful analytical frameworks, creating something akin to a navigable map of the brain, much like a Google Earth for neuroscience. Dr Wanner, together with a dynamic group of imaging and data specialists, is driving this effort forward, positioning PSI at the forefront of a field where technological sophistication and scientific curiosity meet to unlock some of the most complex challenges in modern biology.

How is the current geopolitical environment reshaping international scientific collaboration, and what does this mean for PSI's mission and ability to attract top talent?

The increasingly unstable global landscape has placed considerable strain on international scientific cooperation. While institutions in countries like Switzerland may attract individual researchers seeking more stable environments compared to markets like the US where recent political shifts have created uncertainty, this is not a development to celebrate. What we are witnessing is a widespread retreat from the open, globally networked model that once defined modern science.

Since the onset of geopolitical tensions between the United States and China in 2018, followed by the COVID-19 pandemic, the war in Ukraine, and the growing ambiguity of the US' role in global research, the entire system has been weakened. Switzerland has not been immune – its three-year exclusion from Horizon Europe not only disrupted funding and collaboration but prompted opportunistic recruitment attempts by other countries. Yet genuine scientific progress cannot be built on such fragmentation.

At its essence, science is driven by collaboration among the most capable minds, wherever they are located. Global challenges in all areas of life science demand cooperative solutions developed

through trust, shared purpose, and scientific alignment. The current trend toward isolation and reduced exchange, while sometimes politically expedient, ultimately compromises the quality and speed of innovation. Although history has shown that defence-driven research can yield technological advances, it is rarely the most effective or inclusive path forward. For PSI, the priority remains clear: to continue fostering open, excellence-based collaboration, even amid global turbulence, because the complexity of the challenges ahead leaves no room for parochial science.

How is PSI integrating artificial intelligence into its research and engineering activities, and what potential does it see in this rapidly evolving field?

AI has already had a transformative impact at PSI, particularly in structural biology, where it has fundamentally changed how protein structures are analysed and predicted. One of the earliest and most powerful examples of scientific AI was AlphaFold, trained on publicly available protein structure data, much of it produced through crystallographic work conducted at PSI and other centres of excellence. Today, more than half of the institute's structural biology research incorporates AlphaFold in some capacity, accelerating discovery and reshaping established methodologies. Crucially, this success underscores the importance of high-quality experimental data as the foundation for impactful AI applications. Looking ahead, PSI sees significant promise in pairing its experimental capabilities with proprietary pharmaceutical data to explore AI-driven drug development in confidential, collaborative settings.

Beyond the life sciences, AI is increasingly embedded across PSI's technical infrastructure. With half of its 2,300 staff focused on engineering and operations, the institute applies AI not only to research but also to the optimisation of its complex instruments, such as the Swiss X-ray Free Electron Laser. These machines involve vast parameter spaces and produce enormous volumes of data, making them ideal environments for AI-driven efficiency gains. In some cases, machine learning models have already improved system performance by orders of magnitude. PSI is now extending these tools into the design phase of next-generation infrastructure, further blurring the line between research institute and high-tech engineering environment. Meanwhile, broader developments in Switzerland, such as EPFL training dedicated AI models on hundreds of thousands of medical research papers, are moving AI closer to the reasoning and language used in scientific practice. As these systems evolve, they are beginning to mirror the analytical capacity of highly trained researchers, making AI not just an assistant but, increasingly, a collaborator in advancing scientific discovery.

What do you consider your proudest accomplishment after five years as Director of PSI, and what are the most significant developments the institute is preparing for in the coming years?

Over the past five years, my greatest sense of accomplishment has come from seeing PSI deliver on its core mission: conceiving, designing, and building the kind of world-class scientific infrastructure that enables breakthrough research. The successful upgrade of the Swiss Light Source and the launch of the IMPACT project are two milestones that exemplify this ethos.

What I find particularly meaningful is that these are not abstract ambitions, we invest in technologies that we believe will shape the future, and we see them realised through instruments that support both fundamental discovery and real-world application. That process of long-term thinking made tangible through technological excellence is what defines PSI at its best.

Looking ahead, PSI is engaged in shaping a forward-looking agenda that stretches over the next decade, with multiple large-scale infrastructure projects already under planning. While securing funding for such endeavours has become increasingly complex in the current climate, we remain committed to maintaining Switzerland's global standing in scientific instrumentation. In parallel, energy research is gaining momentum, with pilot projects in synthetic fuels now underway. Nuclear energy is also returning to the strategic conversation. Switzerland currently operates four reactors across three sites, and unlike some neighbouring countries, has chosen not to impose fixed lifetime limits, focusing instead on rigorous safety criteria. PSI continues to contribute technical insight to help guide future energy policy. Whether through next-generation imaging for life sciences, innovation in energy systems, or the continued development of enabling technologies, PSI will remain at the forefront of Swiss and international scientific progress.

What final message would you share with the international healthcare and life sciences community regarding PSI's scientific potential and future opportunities?

Looking ahead, two scientific frontiers at PSI hold particular promise for transforming biomedical research and pharmaceutical innovation. First, imaging technologies at PSI are rapidly evolving toward resolutions that will allow visualisation of structures as detailed as single cells and entire neuronal networks. These breakthroughs are not decades away – they are imminent, and their implications for understanding complex biological systems are profound. Industry stakeholders

would do well to incorporate these capabilities into their long-term research strategies now, rather than later.

Second, the Swiss X-ray Free Electron Laser is redefining structural biology by making it possible to observe molecular interactions dynamically rather than statically. We are now able to capture sequences showing how drug compounds bind to and dissociate from their targets in real time. These insights offer a fundamentally new perspective on drug mechanisms, yet they remain largely underutilised within pharmaceutical R&D, perhaps because they still feel ahead of their time.

The science is here, the data are compelling, and the opportunity to integrate such dynamic understanding into drug development is real. At PSI, we are committed to pushing the boundaries of what is possible and invite the global scientific and healthcare communities to engage more deeply with the emerging tools and discoveries that will shape the next era of innovation.

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