Insights

Insights #2, September 2024

CRYSTAL CLEAR

THRPTX INNOVATION SUMMIT

Does society accelerate medical innovation?

SCIENCE CALLING

Ultrasound technologies deliver medicine directly to the brain

SOUNDING OUT PATIENTS

Voices in Support of Therapeutic Adherence: Mobilizing, Bearing Witness and Innovating

FUTURES FORUM

The pharmaceutical industry and decarbonization: a difficult equation

TELL ME A STORY

« World Capital for Innovation » : how has the Boston-Cambridge ecosystem built this reputation?

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A magazine proposed by SERVIER

SUMMARY

EDITORIAL

Dear readers, we are back to take a closer look at the major challenges facing our industry in Insights!

For this issue, Dr. David Edwards, professor of bioengineering and founder of start-ups like Foodberry and Le Laboratoire, looks at how societal changes shape medicine and health care approaches, as well as the impact of health care innovations on society.

You'll also find out how start-up TheraSonic is breaking through the protective barriers of the brain with their ultrasound-based technology.

Ever wondered why such a large majority of health care innovation is concentrated in the Boston-Cambridge ecosystem? William Sellers, MIT Broad Institute member and head of Harvard's cancer program; Rachele Ryan, Director of Partnerships at Lab Central; and Nabeel Bardeesy, associate Professor at Massachusetts General Cancer Center, tell us how therapeutic innovation flourishes in this unique place.

When it comes to health care, is it really possible to think about "environmental cost" in the same way as other sectors? Faced with ever-increasing medical needs, Mathis Egnell, engineer in charge of the Shift Project's health program, addresses this question by exploring ways of balancing the objectives of reducing environmental impact and increasing medicine production.

Lastly, did you know that the World Health Organization (WHO) reports that despite major medical advances in recent years, management of chronic diseases remains extremely poor, largely due to low adherence to treatment? In a new podcast co-created with Politico, find out what solutions exist to remove the obstacles to optimal treatment adherence.

Happy reading!

Society as an innovation accelerator?

On June 18, Dr. David Edwards, Professor of Bioengineering, founder of several start-ups, and a specialist in respiratory diseases, took part in «THRPTX», Servier Group's Therapeutics Innovation Summit held at Paris-Saclay. The Insights team had the opportunity to interview Dr. Edwards with a focus on one of the main topics at the event: The relationship between medical innovation and societal expectations.

Insights : Hello David. You recently took part in the Round Table — «How do innovations in healthcare advance our societies?» — at THRPTX, the first international scientific symposium hosted by Servier.
To get started, could you please tell our readers a little more about this topic and what it means to you?

David Edwards : Challenges and opportunities to human healthcare are coming to people very quickly today. Responding to these challenges and opportunities therefore raises the question of how-to bring healthcare innovation to patients more quickly than ever before.

Artificial intelligence (AI) has obviously emerged with incredibly speed as a major opportunity for healthcare innovation — while to some degree a challenge as well. The speed with which AI has come to the fore is dizzying — and the general public expects the healthcare industry to make sense of it, just as quickly.

COVID-19 emerged as a serious threat to human health and global economies with unusually rapid speed. My research, which relates to respiratory health and novel respiratory healthcare technology, placed me amid a pandemic challenge. It also placed aerosol scientists like me, with infectious disease specialists, regulators, public health authorities — at a frontier of science where we were all learning, discovering, and getting familiar with scientific domains that till then had largely existed in academic silos.

The public expected healthcare scientists and the healthcare industry to innovate and solve pandemic challenges — and while success came, it frequently came with public confusion. We must get better at managing fast-paced changes in healthcare innovation.

During THRPTX, numerous experts met at Servier's R&D Institute in Paris Saclay to identify several avenues to explore in the fight against cancer

Insights : Thank you for your comments. If we turn the question the other way round, how would you say social changes are impacting medicine/healthcare today?

D.E : One obvious way in which social changes are challenging human health and healthcare delivery is in the tilting of our lives to digital or virtual activities that bring us extraordinary levels of information, frequently provoking anxiety, and paradoxically shortening human attention span. I am particularly focused on another challenge :

the challenge of climate change to human health.

Here again human airways are at the forefront of the healthcare challenge. As the atmosphere warms up, dehydration of the earth's ecosystems is advancing, and with these ecosystems are human airways. Respiratory health, further challenged by the burning of biomass fuels is very unevenly distributed among the human population. Those at most risk of airway dehydration, and respiratory diseases ranging from asthma to influenza are often those least able to access the best quality healthcare. I raise this mostly to illustrate that as we advance healthcare solutions in this fast-paced era of challenge and opportunity we must be sensitive to the need to get solutions not only to those who can afford it but to those who cannot.

Insights : Going a step further, what role can society play in the emergence of therapeutic innovations?

D.E : For human society to have an impact on healthcare innovation, it must have a voice in healthcare innovation.

Frankly, healthcare innovation will not achieve its optimal goals, of getting healthcare to as many as possible as quickly as possible, without human society taking part in the scientific conversation. Innovation in healthcare tends to be highly guided by human clinical trials and regulatory process — rightfully. However, this process rarely gives patients — healthcare consumers — the voice that the same innovation process does, for instance, in the food sector. It may be that the recent pandemic, during which the public frequently did have a voice (and I would argue that this voice was amplified by the healthcare sector.

Dr. David Edwards: Scientist, Inventor, and Writer

Dr. Edwards is a Professor of Bioengineering at Harvard University's School of Engineering & Applied Sciences. His research led to the startup of Advanced Inhalation Research, leading to the FDA approval of Inbrija, inhaled L-Dopa for the treatment of Parkinson's. His pioneering work on airway hydration led to FEND, named one of Time Magazine's Best Inventions of 2020. Dr. Edwards has been awarded a number of international honors and awards. He is a member of the National Academy of Engineering in the USA and France, a member of the National Institute of Inventors, and a recipient of the Chevalier des Arts et des Lettres from the French Ministry of Culture. He is also the author of books ranging from applied mathematics to fiction and non-fiction, and creator of "Le Laboratoire" in Paris and Cambridge, a lab space for scientists and artists.

Insights : In your opinion, how can we reduce the barriers between the healthcare industry and the general public?

D.E : I believe we should find creative ways to invite the public into the scientific process, help the public understand where healthcare innovations come from, and appreciate the excitement of discovery. If the public remains on the other side of the wall that separates research from marketed product, it will never understand where innovations come from. Given the pace of change today, even more problematic will be the inability of the public to engage with products that are moving very quickly from research to commercialization — as the language of these products will reflect a culture (the culture of innovation and discovery) that the public will be unprepared to understand. I would urge the healthcare sector and scientists to communicate more transparently.

By being more inclusive, we can give patients, caregivers, a chance to receive innovations into their lives more readily, and those of the public interested in research may actually have the opportunity to make their own contributions to healthcare science.

Insights : In the years to come, what innovations do you think could revolutionize patients' lives from a medical point of view? And how can we get ready for them?

D.E : Gene therapy, artificial intelligence, and other breakthroughs in science and technology will alter healthcare in the next ten years. However, most impactful of all, may be relatively simple science innovations that improve human health for the greatest number of people. Our understanding of biology and healthcare processes and materials is now such that we have the chance to redesign nature with nature's own building blocks. This is happening today in my work as we come to understand how our airways adapt to changing atmospheric conditions and elsewhere as in the rich opportunities afforded by emerging understanding of the microbiome.

«THRPTX», the Therapeutics Innovation Summit, is the first symposium hosted by the Servier Group at Paris-Saclay. The event brought together over 200 experts, decision-makers, physicians, researchers, and astute observers to explore major therapeutic advances in oncology, as well as to envision the potential implications for the healthcare ecosystem.

See the event in images

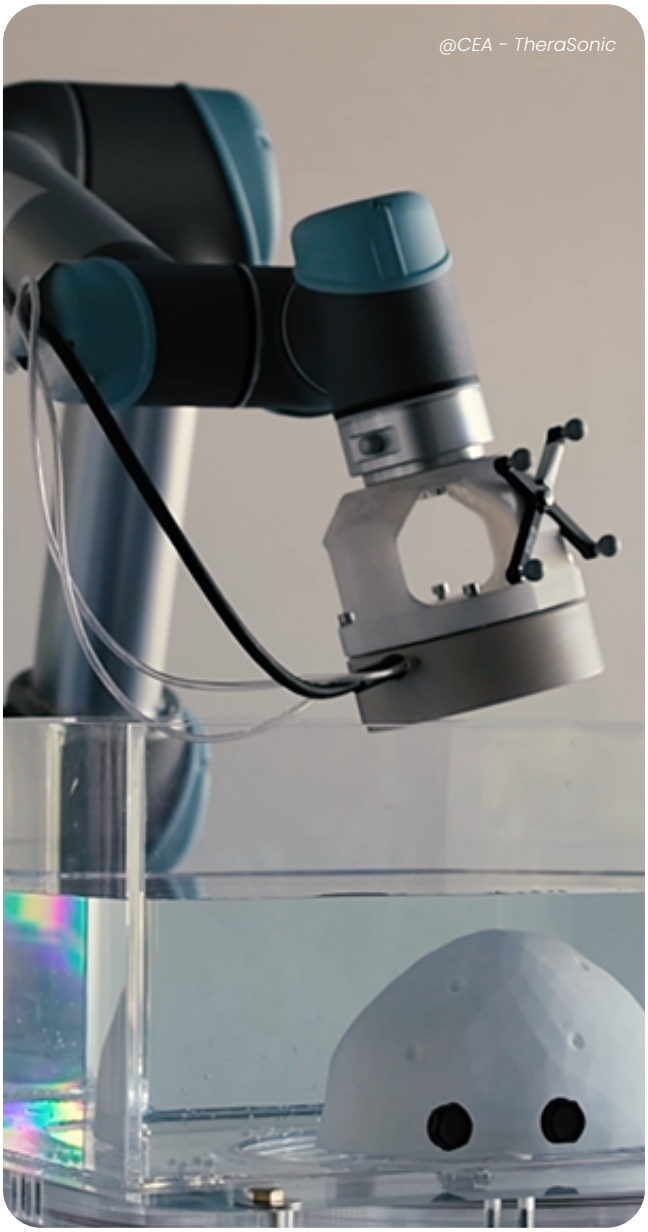
Ultrasound technologies deliver medicine directly to the brain

"Treating patients with brain disease without being invasive." This is TheraSonic's mission, a start-up created in 2023 as an offshoot of the CEA (French Alternative Energies and Atomic Energy Commission). Its co-founder and president, Benoit Larrat, explains how its technology, based on focused ultrasound, delivers therapies without surgical intervention in the brain .

Insights : Hello, Benoît. How is treating the brain a challenge for science? What are the unique features of this organ that make administering therapy so complex?

Benoît Larrat : The brain is unique in that it is an organ that is extremely well-protected from the outside, both mechanically by a solid braincase, and physiologically, by blood exchange systems that are extremely regulated with the extracerebral medium, the ventricles — that is to say cerebrospinal fluid (CSF) — or blood.

The most selective interface is the blood-brain barrier (BBB). Its role is to regulate exchanges between the blood and the brain, and particularly to prevent the pathogens that are potentially present in the bloodstream from entering the brain. The blood vessels found in the brain are distinctive in that they are very tightly sealed. The endothelial cells that compose them are linked together by 'tight' junctions, which are protein junctions that prevent most substances — whether harmful or therapeutic — from passing through.

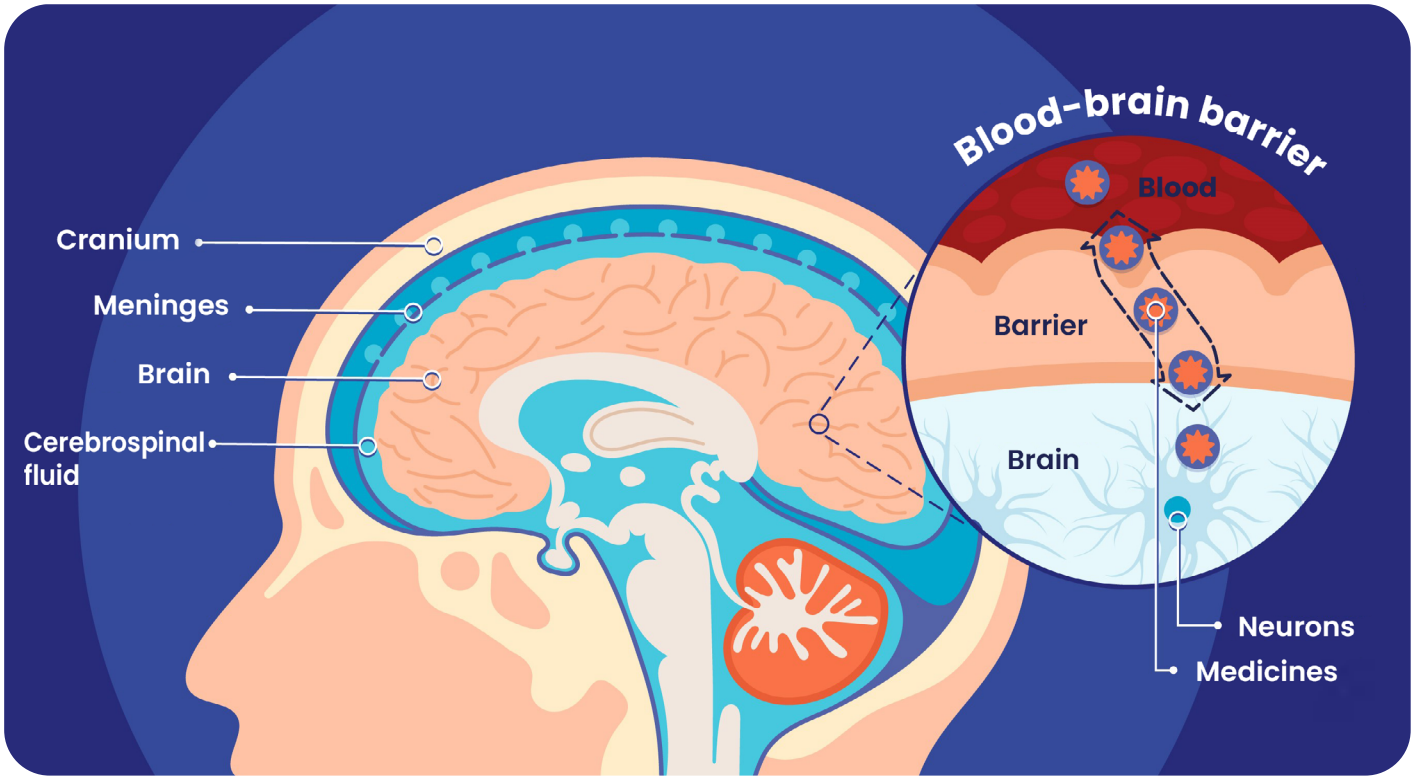


TheraSonic's technology uses ultrasound to transport therapeutic substances to a target located in the brain.

For almost all extracerebral molecules, it is nearly impossible to pass through this barrier. It is estimated that more than 95%[i] of known pharmaceutical molecules cannot make it through to the brain!

Of course, for the brain, the nature of such a protective system is vital from the outset because this protects it from harmful elements. It also helps to ensure stable biochemical conditions in the brain. This is called homeostasis.

Nevertheless, when it comes to treating a patient with a brain disease, such as a tumor or neurodegenerative disease, it is a real challenge to administer the therapeutic molecule to reach targets located in the intracerebral environment. In fact, although I am convinced that molecules exist today to treat most of these pathologies, we are not able to get sufficient quantities of them to the areas they need to treat.



The brain is physically and physiologically protected by several protective barriers, each of which plays a very specific role. These include:

- *Cranial bones*
- *Meninges*
- *The mechanisms regulating exchanges between cerebrospinal fluid-filled cerebral ventricles and the brain*
- *The blood-brain barrier (BBB)*

i: W. M. Pardridge, "Blood-brain barrier drug targeting: the future of brain drug development", Mol Interv, vol. 3, 2003, p. 90–105 (PMID 14993430, read online [archive], viewed on May 16, 2011)

Insights : And so, where does research stand in this area today? What solutions exist to reach the brain, and ultimately, deliver a therapeutic substance within it?

B.L : I would say that currently, the goal is to be able to deliver the right dose of medicine to the right therapeutic target without having to resort to using delivery technology.

Caring for the brain also means balancing the benefit-risk for the patient.

Caring for the brain also means balancing the benefit-risk for the patient, finding the right compromise between the quantity of medicine sufficient and the toxicity induced by treatment. Given the small proportion that accesses the brain, especially for the most promising biotherapies, the peripheral toxicity is what limits the total acceptable dose to be administered to the patient. We must not risk administering a dose that is too high. Much of the effort therefore consists in increasing active ingredients' natural capacity to cross the BBB while limiting their peripheral side effects.

Then, a second point that researchers are actively examining is solving the problem by offering patients new methods of administration, which is our case.

Today, several methods exist to reach brain tissue. These include invasive intracerebral delivery by needle, convection-enhanced delivery (CED), direct injection into cerebrospinal fluid, intranasal nebulization of active ingredients, implants loaded with therapeutic agents, etc. These technologies show some effectiveness but cannot always be implemented. In addition, they suffer from limitations such as invasiveness or lack of targeting. For our part, we have based our approach on transcranial ultrasound technology.

Did you know?

As a committed player in the fight against cancer, Servier joined the Paris-Saclay Cancer Cluster (PSCC) in November 2023.

Claude Bertrand, Executive Vice President Research & Development, Chief Scientific Officer, sits on the Board of Directors, and several Group employees have also joined the biocluster's scientific committees of governance or working groups to provide their expertise in the field of oncology.

Insights : Tell us about your technology. How does it work? How could ultrasound allow a therapeutic molecule to reach its target?

B.L : Our technology is a drug delivery system, like the systems discussed above. Its purpose is to transport therapeutic substances to a target located in the brain.

Our approach consists of emitting ultrasound in a pulsed manner, which will increase the permeability of the blood-brain barrier locally for a time (T) long enough to allow the therapeutic substance to be administered to the patient.

In very concrete terms, the patient receives microbubbles of air intravenously, which are already used as contrast agents for ultrasound. These bubbles will oscillate under the effect of ultrasound. In contact with the walls of the cerebral blood capillaries, they will generate stress inside the vessels, which will induce a temporary opening of the tight junctions. Ultimately, this allows therapeutic substances a much better passage in this location. Depending on the type of medicine, brain concentration can be increased 2 to 20-fold compared to normal.

The field of application is vast. Our technology can transport all classes of therapeutic molecules to the brain: small molecules, nanoparticles, therapeutic and targeted antibodies, as well as viral vectors for gene therapies, with the objective of treating neurodegenerative or rare diseases, cancers, or psychiatric diseases.

Insights : What exactly does your technology bring to this field and how is it beneficial for the patient?

B.L : The first advantage of an ultrasound approach, and the most important criterion for us, is that it is non-invasive for the patient and offers a simpler care pathway. Indeed, after extensive discussions with health care professionals, many raised the point that patients were reluctant to proceed with treatments that were too invasive both physically and mentally (the duration of the procedure, or even the fact of having to shave their head!). This is key to getting patients to adhere to these treatments.

Our technology therefore takes place in outpatient medicine: one hour is enough for the patient to receive their treatment via ultrasound.

Next, the helmet we are developing is equipped with a dosimeter, which adapts the intensity of the treatment to the patient's skull thickness and each treatment point. This precise approach will help better calibrate the dose of therapeutic substance administered to the patient, and ultimately deliver the most appropriate treatment for both adults and children.

Finally, to aim accurately and treat multiple brain volumes automatically, we rely on a robotic arm that precisely controls the ultrasound beam to scan the areas to be treated, which are determined by physicians according to the patient's medical images.

What are the next steps in developing this solution? In other words, how soon can patients with brain diseases expect to benefit from this medical approach?

B.L Today, we are still in the pre-clinical phases, and we hope to be able to submit a dossier to set up a clinical study in 2025. To this end, we have just finalized an initial fundraising campaign of nearly one million euros from the venture studio M2care and Gustave Roussy Transfert.

We are fortunate to be working within the Paris-Saclay cluster, an ecosystem that is particularly rich and stimulating for the development of innovations in the health care sector. We are convinced that as a start-up, collaboration with other partners is essential to the development of our technology.

We are also stakeholders in the Paris-Saclay Cancer Cluster, an oncology cluster made up of public and private players from the Paris-Saclay geographical area. Its mission is to accelerate innovation in cancer treatment by providing an ideal framework (mentors, network, funding, clinicians, data, samples, technologies, infrastructures and laboratories) in which to develop innovative projects in the field of oncology.

Benoît Larrat

Benoît Larrat is a graduate of ESPCI Paris in Physics and holds a doctorate in Medical Instrumentation. He did his post-doctorate at NeuroSpin on ultrasound as a delivery route of substances to the brain. A tenured CEA research engineer since 2012, he developed this technology in animals by collaborating with several other academic and industrial laboratories. In 2020, the TheraSonic project integrated the CEA's technological maturation and spin-off program. Together with his co-founder Anthony Novell, a researcher at CNRS, he designed and developed a prototype medical device based on previous work. At the end of 2023, TheraSonic officially launched and carried out its first fundraising campaign. The start-up's objective is to validate this technology as quickly as possible on the first patients in neuro-oncology, then to establish pharmaceutical partnerships in order to demonstrate the added value of the approach combining innovative biotherapies and ultrasound.

Pharmaceutical industry and decarbonization: A difficult equation

To reach decarbonization goals, the majority of the savings that can be achieved within the pharmaceutical industry lie in the value chain and medicine production. From optimizing transport to artificial intelligence and eco-design, here are some possibilities for how decarbonization can go hand in hand with improvements in health care quality.

Reducing emissions: A major challenge

The pharmaceutical industry faces a challenge on two levels. On the one hand, it must maintain a high standard of care for patients, as the global population is aging – especially in developed countries – and therefore has greater health needs. On the other hand, it must limit its environmental impacts.

The pharmaceutical industry accounts for 4.4% of CO_2 emissions globally[i], and significantly more in developed countries (7.6% in the United States, 6.4% in Japan, 5.4% in the UK and 5.2% in Germany[ii]).

Of these, 75%[iii] are indirect, meaning that they are linked to the value chain: production, transport, medical devices, equipment and technologies, instruments, etc.

If no action is taken and this becomes the status quo, things could deteriorate rapidly — the pharmaceutical industry could see its carbon footprint triple by 2050.[i]

To reduce its emissions all while remaining efficient, the pharmaceutical sector has several options, including optimizing its value chain and capitalizing on breakthrough innovations.

Shipping is one way of reducing greenhousve gas emissions

i: UPSTREAM SCOPE 3 EMISSIONS ACROSS THE PHARMA INDUSTRY, may 2023v
ii: THE PHARMACEUTICAL INDUSTRY'S CARBON FOOTPRINT AND CURRENT MITIGATION STRATEGIES: A LITERATURE REVIEW, IPSOR annual 2023
iii: Accelerating the transition to net zero in life sciences, McKinsey, August 2023

Options for reducing the sector's emissions
First step: Optimizing the production chain

Most emissions are linked to the value chain, so this is where the first opportunities for decarbonization lie. One avenue to explore would be to relocate manufacturing facilities so that they produce medicines as close as possible to the place of consumption. This would make it possible both to decarbonize and to meet patients' needs more quickly.

Mathis Egnell is an engineer in charge of the health program at The Shift Project, a think-tank working to mitigate climate change and reduce the economy's dependence on fossil fuels and oil in particular. He believes that indicating the carbon content of each medicine would be a good idea.

"In the UK, the National Health Service (NHS) has drawn up a roadmap to bring its suppliers on board and work toward this.
From 2028, it plans to require drug manufacturers to publish their carbon content in order to be able to access the British market. France is also taking similar steps. However, it would be even more relevant to take action at the European Union level, for greater impact."

Another way of decarbonizing the value chain is to opt for more environmentally responsible means of transport, energies, and buildings. For instance, six of the Servier Group's 16 industrial sites now use 100% renewable electricity, generated by on-site solar panels or sourced externally.

Mathis Egnell

Engineer, in charge of the health program at The Shift Project

After graduating as an engineer from Mines and AgroParisTech, Mathis Egnell began his career as a network environmental footprint consultant for the World Health Organization before joining The Shift Project, where he is now in charge of the health program.

Did you know?

Servier now prioritizes the use of maritime freight to ship its medicines. In 2022-23, 57% of its intercontinental shipments were transported by boat, which represents a 12% increase in maritime transport and a 4% decrease in air transport compared with the previous year.

Second step: Capitalizing on breakthrough innovations like artificial intelligence AI and eco-design to decarbonize health

To decarbonize the health industry, and production of medicines in particular, breakthrough technologies that promise to deliver major gains in terms of efficiency also have a role to play.

As an example, **generative AI** can be used to accelerate the time it takes to develop medicines. This technology can be used to identify the most promising molecules and simulate their interactions on various scales, with approaches based on phenotypes (all of an organism's observable traits) and genomes (all of an organism's genetic material). This makes it possible to increase the number of potential drug candidates and reduce the risks of failure.

For example, a study by Nvidia and Recursion Pharmaceuticals made it possible to test — in one week — a quantity of molecules that it would have taken 100,000 years[iv] to test using traditional methods. Elsewhere, Insilico Medicine used generative AI to develop a medicine to treat a lung disease. It claims that use of this technology enabled it to develop its product in two and a half years instead of six, while dividing the cost by 10.

What's more, AI can be used to improve diagnostics and therefore limit waste, because a correctly diagnosed patient is treated more quickly, for example, for endoscopy and reading x-rays. To demonstrate this, a Swedish study proved that using AI to support reading mammograms helped radiologists to detect 20% more breast cancers[v].

"The sustainable transformation of the pharmaceutical industry represents an unprecedented challenge that calls for unique responses. R&D programs and manufacturing processes are subject to strict regulations. These priorities in terms of safety limit our flexibility and any changes to our practices take time. We are constantly looking to achieve the perfect balance between ecological goals, patient interests and health requirements. To do this, we need to ensure that strategies are aligned and establish collaboration that takes into account the interests and outlook of all stakeholders (patients, suppliers and partners)."

Shuo Wang,
CSR Manager, Servier

iv: *Forbes : https://www.forbes.com/sites/bernardmarr/2024/06/19/how-generative-ai-is-accelerating-drug-discovery/*
v: *RSNA Artificial Intelligence Evaluation of 122 969 Mammography Examinations from a Population-based Screening Program : https://www.thema-radiologie.fr/actualites/3239/nouvelles-preuves-de-la-pertinence-de-l-ia-pour-le-depistage-du-cancer-du-sein.html*

The eco-design of medicines is another area worth looking into. This includes the use of green chemistry for drug synthesis or, at the end of the value chain, the choice of eco-friendly materials for packaging. This is the principle behind Servier's EcoDesign program, launched in 2020. It has set sights on 100% of its new medicines to incorporate eco-design principles into their packaging by 2025, and 100% of new drugs to be eco-designed by 2030.

By combining the optimization of existing processes with breakthrough innovations, equally good or even better care can be provided, with a significantly lower impact on the environment. But to achieve it, all industry stakeholders must work together with a view to achieving this. Fortunately, awareness of this challenge is gaining ground and a number of countries are taking action to provide greener health care for their populations. The US Department of Health intends to reduce its emissions by 50% by 2030 and achieve neutrality by 2050. In the UK, the NHS is aiming to be carbon neutral by 2040, while the issue of decarbonization is also being examined at in countries like India, China and Japan. By continuing to raise efficiency levels and innovate, the pharmaceutical industry is positioned to be a valuable ally to reach these goals.

To meet the challenge of decarbonizing the pharmaceutical industry, Servier has set ambitious goals: reducing its scope 1 and 2 emissions by 42% and scope 3 by 25%.

To achieve this, Servier is building its low-carbon strategy around four core pillars:

Reducing energy consumption, while increasing the percentage of renewables in its energy mix

Rethinking how we travel, while increasing the percentage of hybrid and electric vehicles used

IIncorporating a sustainable dimension into the criteria for selecting suppliers of goods and services

Promoting the use of more sustainable means of cargo transport (e.g. maritime transportation)

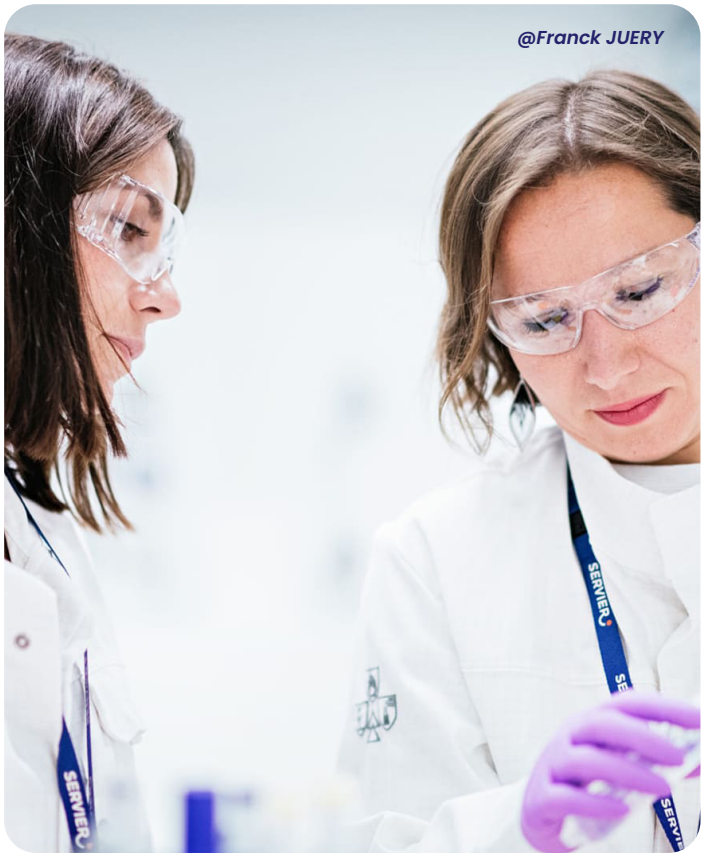
Scope 1 emissions occur directly from sources that are controlled or owned by the Group.
Scope 2 emissions are associated with the purchase of electricity, steam, heat, or cooling.
Scope 3 emissions include greenhouse gas emissions that are not directly related to producing the product but are caused instead by other stages of the medicine life cycle.

World Capital for Innovation: How has the Boston-Cambridge ecosystem built its reputation?

With 10 million square meters of research laboratories, the Kendall Square ecosystem in Cambridge, Massachusetts, has the world's highest concentration of scientific population per square meter. Over the last century, Kendall Square has seen a number of transformations, closely linked to the history of the Massachusetts Institute of Technology (MIT). Let's take a look back at the changes that have led to it becoming a preeminent hub for biotechnologies.

01 First steps: All systems go, paving the way for innovation

Kendall Square, today a world-renowned innovation hub, was nevertheless not destined to become its global capital. Its story begins in 1916, when MIT (Massachusetts Institute of Technology), the prestigious American university specialized in science and technology, wanted to expand its borders. A new building was built in an abandoned former industrial area, with one ambition: to create the leading center for scientific and technological education. This marks the stirrings of Kendall Square.



In the years that followed, MIT opened various research centers, which progressively covered all groundbreaking scientific and technological fields, from IT to aeronautics. In 1974, it inaugurated one of the world's first cancer research centers.

02 1970s: A decade of contrasts for scientific innovation

In the early 1970s, researchers from MIT manage to isolate the components of DNA. This scientific revolution would pave the way to the discovery of pioneering treatments for diseases previously believed to be incurable.

However, it also raised concerns about the dangers surrounding control of human genetics. Work relating to DNA was suspended for two years at Kendall Square. This is the time that it would take the government to define a legal framework ensuring that research work is carried out for the benefit of the greater community.

Servier's office in Boston is located in th innovation ecosystem of Kendall Square

Rachele Ryan

Rachele Ryan is the director of partnerships at LabCentral. She has more than a decade's experience matching high-potential startups with contacts within Boston's innovation ecosystem. Prior to joining LabCentral, Rachele Ryan led the MassCONNECT mentoring program at MassBio, the Massachusetts biopharma industry association. Previously, as part of the International Business Development team at the Consulate General of Canada in Boston, she assisted Canadian companies with their expansion efforts into New England and supported fast-growing startups participating in the Canadian Technology Accelerator in Boston (ATC@Boston).

> *The biotech ecosystem in Cambridge, and in Kendall Square in particular, represents an industrial density found nowhere else in the world. Strategically located between MIT and Harvard, Kendall Square is also home to leading pharmaceutical companies, a large number of biotechs, venture capital firms, industry associations, etc. It's a flourishing ecosystem, with everything that our local startups might need for their innovations to be made available to patients. While it is not essential for biotech startups to be based in Cambridge, many high-potential companies choose to make it their home in order to benefit from easy access to the resources and potential employees located in this community.*
>
> Rachele Ryan,
> Director of Partnerships, LabCentral

03 Kendall Square's golden years: Scientific revolution moves forward

Kendall Square becomes the first place — and the only place — in the world to benefit from a legal framework governing scientific research revolving around DNA. This would enable the biosciences community to flourish in this hub. This exceptional setting, coupled with the first significant results achieved by the research centers at this innovation hub attracted new companies, new biotechs and the most distinguished researchers every day. They were all looking for the best place, the right research platforms and a network of experts who share the same vision: innovating for therapeutic progress.

The arrival of private sector players also marks a new approach to research: that of the "academic entrepreneur" culture. The aim is no longer to conduct research for the sake of research, but to guide and direct the work with a view to delivering these solutions to patients. Private sector players contribute not only to funding this work, as in the example of the Whitehead Institute (a renowned institute specialized in biomedical research), but also industrializing this sector. Pharmaceutical companies are then able to open up quicker access to treatments for patients.

In the space of just a few years, the Boston-Cambridge innovation hub grew from being a handful of businesses to comprising thousands of stakeholders. This concentration of disruptive and innovative players led to the development of the first recombinant DNA research by the company Biogen in the early 1980s. It was a global scientific revolution, which would be followed by many others: human insulin, growth hormones and even the emergence of cancer treatments.

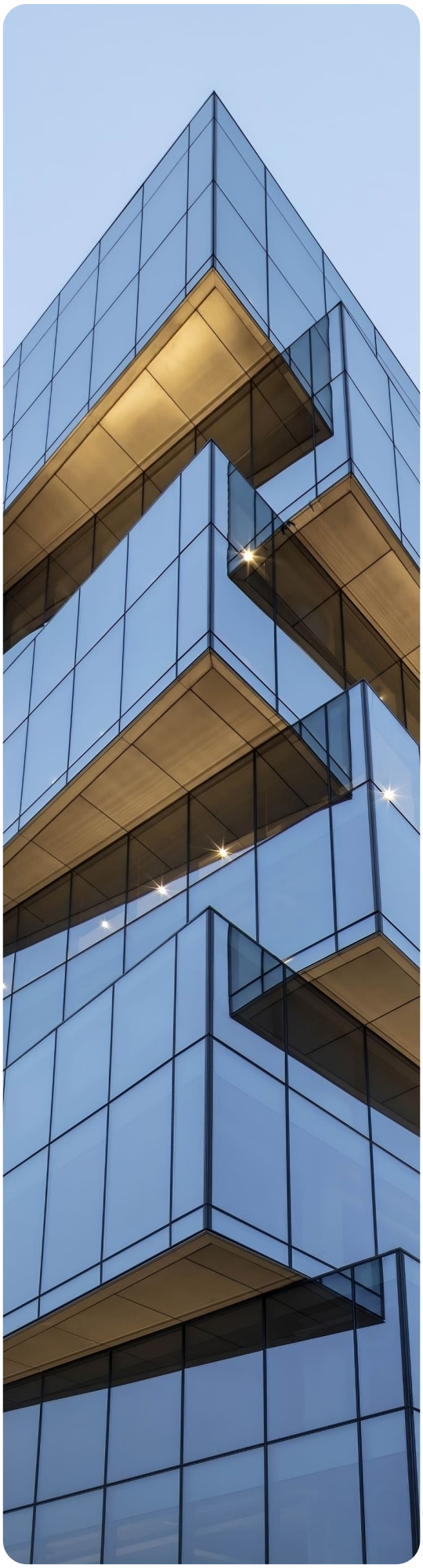
04 Biogenetics pioneers

Biogenetics was a new scientific discipline in the early 1980s. For researchers, it involved seeking to identify the causes of a disease (mutations, specific cellular mechanisms, etc.) rather than its symptoms.

When Biogen was created, the company's founders, Walter Gilbert and Charles Weissmann, committed to relying on biotechnologies to develop therapeutic solutions for diseases with unmet needs. However, as this was a new discipline, there were few experts around the world. To achieve this goal, Biogen brought together the most renowned researchers in this field.

Their initial results were more than promising: Biogen would file a patent for the first chemical synthesis solution for the interferon alpha gene. Thanks to this innovative process, treatments for hepatitis B and certain forms of cancer, such as hairy cell leukemia or Kaposi's sarcoma, were successfully developed.

> *Founded in 2013, LabCentral has been a pioneer within the life sciences startup ecosystem, introducing shared laboratory spaces and establishing new standards for industry support. LabCentral has further strengthened its presence, with over 20,000 square meters across six cutting-edge technological facilities, offering essential resources and infrastructures for 278 new innovative businesses. Part of Kendall Square, LabCentral is strategically positioned at the heart of this biotech innovation hub, facilitating technology transfers from local universities to startups. Thanks to strategic partnerships set up with pharmaceutical groups such as Servier, LabCentral offers these startups access to essential feedback as well as opportunities to develop potential collaborations, helping support scientific discoveries in the life sciences sector.*
>
> *The success of LabCentral illustrates the vital impact of collaborative innovation in the life sciences sector. By clearing barriers, encouraging collaboration, and providing vital support for startups, LabCentral is continuing to stimulate scientific progress and shape the future of biotechnologies.*
>
> Rachele Ryan,
> Director of Partnerships, LabCentral



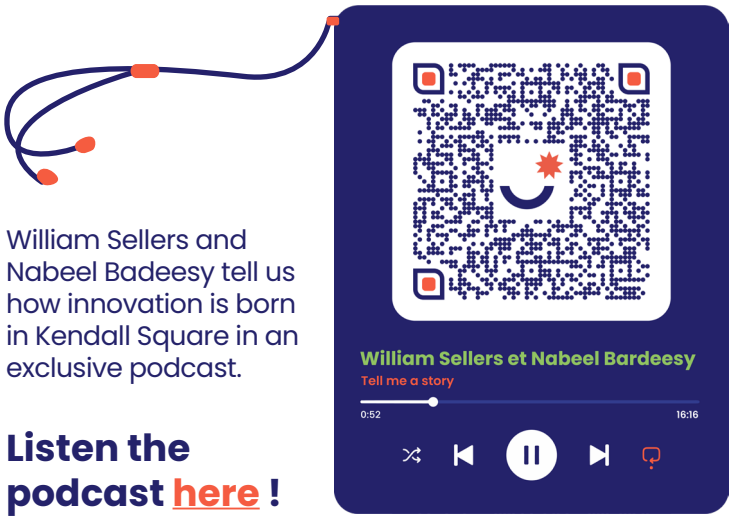
Servier's office in Boston is located in th innovation ecosystem of Kendall Square

05 Kendall Square today: A dream environment for biotechs

At Kendall Square, innovation is not only encouraged, but also expected. Today, this innovation hub — the only one of its kind worldwide — brings together over 1,000 companies, some of America's leading universities (MIT, Harvard), internationally-renowned pharmaceutical companies, the five GAMAM (Google, Apple, Meta, Amazon and Microsoft), various research centers in all fields, and world-class biotech incubators (LabCentral and The Engine).

These biotechs could not hope for a better environment to support the development of their research work. Having so many renowned specialist players nearby allow them to benefit from the best counsel: the culture of sharing with peers reduces the risk of failure, capitalizing on shared experience and shared wisdom.

Biotechs are also strategically positioned to identify the needs of pharmaceutical stakeholders, especially in terms of technological platforms.



William Sellers and Nabeel Badeesy tell us how innovation is born in Kendall Square in an exclusive podcast.

Listen the podcast here !

i : « Expérience partagée, sagesse partagée »

06 What does the future hold for Kendall Square?

Artificial intelligence (AI) has opened up a wide range of new possibilities. Every day, Kendall Square players are working to develop and master these new technologies with a view to developing tomorrow's medicine.

Every day, the health companies operating out of Kendall Square are tackling challenges in order to bring solutions to patients with unmet medical needs. The concentration of all these private and public stakeholders involved in research in one location represents an outstanding accelerator for the development of innovative therapeutic solutions. The next 30 years look promising!

Did you know?

The Servier Group has been active in the Boston-Cambridge ecosystem since 2018.

Convinced that open innovation is essential to accelerating research and offering each project the best development framework, the laboratory signed nearly 70 strategic partnerships with private or public stakeholders during the 2022-2023 financial year.

And to press on in this open dynamic, since 2023, the Group has moved all its R&D teams to the Paris-Saclay campus to bring them together in one place in France at its Institute. The Servier Research and Development Institute in Paris-Saclay represents a major step for Servier in building a more open, dynamic and productive research environment for the benefit of patients. It embodies and stimulates Servier's ambition to offer patients cutting-edge therapeutic innovations

The innovative ecosystem at the Paris-Saclay campus was not chosen at random. Like Boston-Cambridge, it is considered one of the most dynamic in the world. It currently accounts for 15% of French research (in terms of the number of researchers) and 40% of private and public research jobs in the Paris region. Eventually, it is expected to account for 25% of French research.

Learn more at *https://servier.com/en/research-innovation/research-development/the-research-and-development-institute-in-paris-saclay/*

Key Figures

The drug development pipeline for the State of Massachusetts (USA) on its own represents nearly half of the total pipeline for China

Massachusetts' pipeline makes up almost

15 %
of the US pipeline

6,5 %
of the global pipeline

Nearly **18 000**
job offers were published in 2023 in the biopharmaceutical sector in Massachusetts

Massachusetts is home to

25 % of the headquarters of all US biotechs

34 %
of the Massachusetts pipeline is focused on oncology

Massachusetts companies account for

33 % of R&D spending in the US

Source : 2023 Industry Snapshot (readymag.website)

Biographies

William Sellers

William Sellers is a distinguished cancer scientist. He is a member of the Broad Institute of MIT and Harvard, where he leads the institute's cancer program. He is also a faculty member at Harvard Medical School (HMS) and senior advisor to the president for experimental therapeutics at Dana-Farber Cancer Institute (DFCI).

He has been recognized with numerous awards, including the Novartis Excellence Award for Innovation, the Abbott Bioresearch Award, the Tisch FamilyOutstandingInvestigatorAward,andtheNationalInstitutesofHealth Physician-Scientist Award. He is renowned among other achievements for his work with Matthew Meyerson on cancer genome sequencing, which paved the way for EGFR-inhibiting drugs becoming standard-of-care for patients.

Previously, William Sellers was also an investigator with the DFCI and associate professor of medicine at HMS. He then served as vice president and global head of oncology for the Novartis group.

Nabeel Bardeesy

Nabeel Bardeesy is associate professor of medicine at Harvard Medical School and assistant geneticist at the Massachusetts General Hospital Center for Cancer Research, and an associate member of the Broad Institute. He has more than 20 years of cancer research experience.

He holds a leadership role in a number of program initiatives in this area, including serving as co-PI (co-Principal Investigator) of the Harvard SPORE (Specialized Programs of Research Excellence)NCI /P50 (NCI – the National Cancer Institute in Gastrointestinal Cancer, Project Leader in a long-standing Program Project Grant (NCI/P01) on the Biology of Pancreatic Cancer, PI of two DOD (Department of Defense) Translational Team Science Awards for biliary cancer, and until recently, served as Director of the Scientific Advisory Board of the Cholangiocarcinoma Foundation. He has been awarded multiple NCI-R01 grants on GI cancer.

Dr. Bardeesy has an extensive track record mentoring future independent investigators. Many of his postdoctoral trainees have received major mentored fellowships and several have obtained tenure track positions in top academic institutes or have gone on to be group leaders in industry.

> *LabCentral is a dynamic environment within which we are constantly innovating to provide better support for our local businesses and our community. In addition to offering cutting-edge equipment, a community, mentoring and many other things, we are working to address an issue relating to representation at the industry level thanks to LabCentral Ignite. This innovative program aims to reduce systemic racial and sexual inequalities in the life sciences field. From pharmaceutical companies to industry leaders, STEM students and entrepreneurs driving revolutionary innovations, LabCentral Ignite is a unique platform that aims to enhance the value of the talents that have always been underrepresented in our sector. Diversity supports innovation and is essential for the future development of LabCentral and the life sciences sector.*
>
> Rachele Ryan,
> Director of Partnerships, LabCentral

Voices in support of therapeutic adherence: mobilizing, bearing witness and innovating

In today's world, where health is of most importance, therapeutic adherence represents a major challenge. To shed light on this issue and offer innovative solutions, the international political journalism organization Politico launched a series of exclusive interviews in collaboration with Servier Group. Here's a look at the main takeaways.

Mobilizing to raise awareness

Currently, over half of chronically ill patients do not take their medications as prescribed[i]. The impact of this on their health and quality of life is often underestimated. Furthermore, lack of adherence significantly affects the costs incurred by health care systems worldwide.

Did you know ?

The World Health Organization (WHO) defines therapeutic adherence as the extent to which a person's behavior – taking medication, following a diet, and/or making lifestyle changes – corresponds to recommendations agreed with a health care provider.

The problem is particularly complex when it comes to chronic diseases, notably cardiovascular diseases. These account for 1.7 million deaths a year in the European Union, or around 37% of all deaths[ii]. Yet up to 50% of patients with chronic diseases do not adhere to their treatment[iii].

The WHO, the OECD and the European Commission have therefore issued a call for action. In Europe alone, better adherence could save around 200,000 lives every year and alleviate costs to health care systems and society[iv] by €125 billion.

i : *Adherence to Long-Term Therapies: evidence for action. World Health Organization 2003*

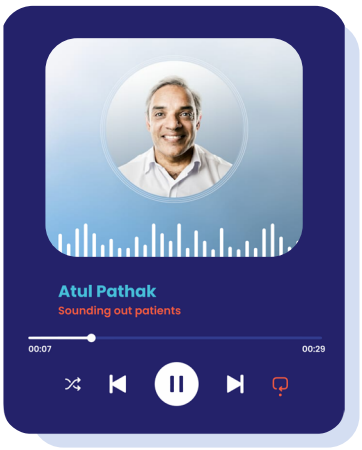
ii: *Timmis et al., 2022 https://www.eea.europa.eu/publications/beating-cardiovascular-disease#:~:text=It%20is%20the%20most%20common,2022%3B%20WHO%2C%202022).*

iii: *Fred Kleinsinger (2020), "The Unmet Challenge of Medication Nonadherence", The Permanent Journal 22. DOI: 10.7812/TPP/18-033. Accessed 12 September 2023*

iv. *Institut Sapiens (2023), Améliorer l'adhésion thérapeutique : un enjeu de santé publique. Available in French at: https://www.institutsapiens.fr/wp-content/uploads/2023/06/Ameliorer-ladhesion-therapeutique-V1.pdf Accessed 12 September 2023*

Bearing witness: Perspectives to gain understanding and take action

To better understand the sometimes complex reasons for a patient's non-adherence, Politico created a series of podcasts featuring health care professionals and patient association representatives. Through captivating interviews, the issue of therapeutic adherence is tackled from different angles, allowing renowned experts to share their knowledge and experiences and also offer best practices to help patients adhere to their treatments.

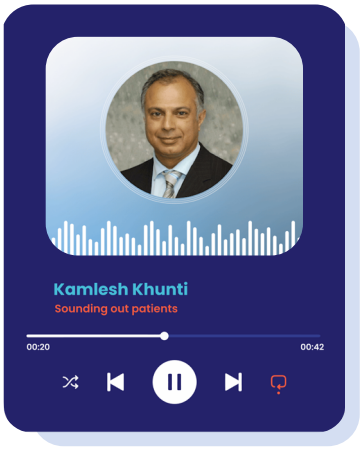


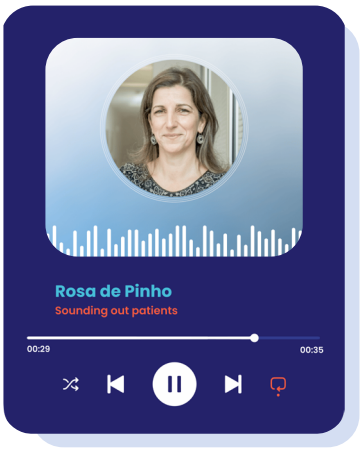
Atul Pathak, MD, PhD, Cardiologist and Pharmacologist at Princess Grace Hospital in Monaco

Read the full interview here:
https://insights.servier.com/wp-content/uploads/2024/07/1_Atul-Pathak.mp4

Kamlesh Khunti, Professor of primary care diabetes and vascular medicine at the University of Leicester in the U.K

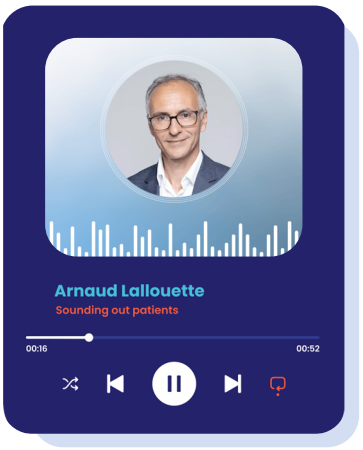
Read the full interview here:
https://insights.servier.com/wp-content/uploads/2024/07/2_Kamlesh-Khunti.mp4





Rosa de Pinho, general doctor, and a hypertension consultant at USF Vale do Vouga in São João da Madeira

Read the full interview here:
https://insights.servier.com/wp-content/uploads/2024/07/3_Rosa-De-Pinho.mp4

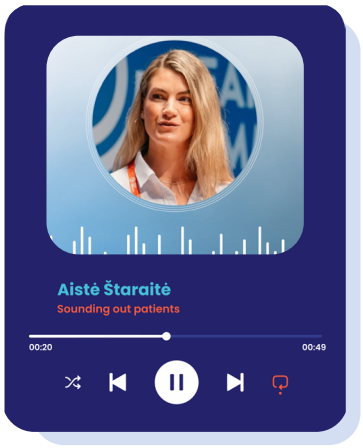


Arnaud Lallouette, Executive Vice President, Global Medical & Patient Affairs, Servier

Read the full interview here:
https://insights.servier.com/wp-content/uploads/2024/07/4_Arnaud-Lallouette_13march.mp4

Aistė Štaraitė, the development executive and council lead for Heart Failure, as well as past chair of the Heart Failure Patient Council, at the Global Heart Hub

Read the full interview here:
https://insights.servier.com/wp-content/uploads/2024/07/5_Aiste-Staraite.mp4



Innovating to improve patient health

The initiative undertaken with Politico aims to bring about tangible changes in how therapeutic adherence is approached. By providing valuable information along with varied yet complementary perspectives, the conversations that Politico and Servier have engaged in strive to inspire concrete, collective actions to improve quality of care and patient well-being.

In addition, by working with patients and forming partnerships with them and the associations that represent them, health care providers will be able to find solutions to counter lack of therapeutic adherence. Arnaud Lallouette, Cardiologist and Executive Vice President of Global Medical & Patient Affairs for Servier, shares his insights: “Patients today are increasingly taking charge of their health and are fully involved in this ecosystem. They inspired us and pushed us to work not only for them but also with them, as early as possible rather than in the later stages when treatments are already available on the market. That makes sense because they live with their disease, they know their own needs and they want to be involved in the treatment they receive. They are experts in the disease and its burden.”

Learn more: Therapeutic adherence, the missing piece to treat chronic diseases

Les Single Pill Combinations (SPC) also represent a major innovation in the daily lives of patients with a chronic disease such as hypertension, diabetes or dyslipidemia. SPCs are medications that combine several treatments in a single pill. They make it easier for doctors to prescribe treatments and for patients to take their medications, thus promoting therapeutic adherence. SPCs are an important breakthrough enabling patients to take better control of their disease and to prevent possible complications.

Learn more: Single Pill Combinations: A solution to foster therapeutic adherence

Servier believes that therapeutic adherence is one key to improving the efficacy of treatments to serve patients. As the world's fifth largest pharmaceutical company specializing in cardiology[v], Servier has made therapeutic adherence one of its top priorities.

Raising awareness for collective action

The partnership with Politico is part of a series of initiatives undertaken by the Servier Group to raise awareness on the importance of adherence in the health care sector. For example, at an event organized at the European Parliament on January 30, 2024, Servier teamed up with learned societies, patient associations and several stakeholders in the health care industry to sensibilize on therapeutic adherence as widely as possible. The initiative was repeated on May 28 at the World Health Assembly organized by the WHO in Geneva.

Did you know ?

In its report on non-communicable diseases, the European Parliament defined adherence to treatment as a "crucial point in the European strategy against non-communicable diseases[vi]." The report urges EU member states to take this issue on board and define ambitious policies in this area.

v : *IQVIA, Analytics Link / World 75 countries – MAT Q3-2023*

vi: *Report on non-communicable diseases (NCDs), European Parliament (2023). Available at: https://www.europarl.europa.eu/doceo/document/A-9-2023-0366_EN.html*