



Dr. Alexander Straub: successful cardiovascular researcher

Passion yields **promise**

The road to approval of a new medication is long and arduous – with lots of surprises along the way. This is why pharmaceutical researchers in particular need the freedom to continually try out new approaches. Dr. Alexander Straub, a chemist through and through, has taken this dictate to heart. His work has made vital contributions to optimizing rivaroxaban and riociguat, two promising active substances from cardiovascular research.

Inventions are always surprising – yet targeted research strategies are vital tools for achieving them. “When seeking success in research, one must have a high level of frustration tolerance,” warns Dr. Alexander Straub, a scientist involved in pharmaceutical research at Bayer HealthCare in Wuppertal. The chemist knows what he is talking about. As one of Bayer’s successful inventors, the 51-year-old has experienced firsthand all of the highs and lows of day-to-day research.

But taking the rocky road paid off in the end, for example with rivaroxaban. “Despite intensive chemical processing, even the strongest compound from the screening was not suitable for oral administration,” recalls the chemist. He therefore took a courageous step backward to resume active substance research. To his great surprise, using the weakest compound as a starting point led him to a breakthrough – and launched a success story. Marketed under the brand name Xarelto®, rivaroxaban is now approved in numerous countries for prophylaxis of venous thromboembolism in patients following elective hip or knee replacement surgery. This means it is administered after major orthopedic surgery to pre-

vent dangerous blood clots. In addition, doctors are now conducting large-scale studies to determine if rivaroxaban offers advantages over the medications currently in use for prevention and treatment of other diseases caused by blood clots.

Award-winning career: scientific rigor pays off

In 2009, rivaroxaban received the German Future Prize awarded by the German Federal President for technology and innovation. Straub has been honored with the Otto Bayer Medal, the highest internal award for Bayer researchers, not once but twice: in 2006 for rivaroxaban, and 2 years later for his role in the development of riociguat. This new active substance from Bayer is currently in clinical testing for treatment of pulmonary hypertension. Straub’s untiring devotion to research played an important role here as well.

The chemist could hardly have hoped for such striking success when he synthesized the first test compounds for rivaroxaban and riociguat in the 1990s. On the contrary: “Failure is the norm for us – but that builds character,” asserts Straub. This comes as

no surprise, however. The library from which the Bayer researchers select suitable “medication blanks” via high-performance methods contains nearly three million chemical substances. Following initial tests with the biological target molecule, the number of remaining hits can range anywhere between one and 10,000. This is where Straub and his team of “active ingredient hunters” in Medical Chemistry come in. Chemical expertise, experience and computer-aided methods for calculation of molecule properties guide these important steps in the active substance selection process. Which structures offer the best basis for development of a medication? “If you bet on the wrong horse, the entire project goes down the tubes,” cautions Straub. The task at hand is to select methods of synthesis for gradually altering the structure until strength, solubility, tolerability and a wide range of other

Passionate chemist: Bayer scientist Dr. Alexander Straub (photo, left) prepares a solution for the rotary evaporator. After the success story of Xarelto®, he is now working with his team (photo right, left to right) – Siegfried Lindner, Sabine von Kathen, Andreas Fehst, Nicole Tesch and Dr. Heinrich Meier – on new indications in cardiovascular research.





Scientific down-time: the time spent away from work belongs to the family. For relaxation, Dr. Alexander Straub likes to get on his bike and cycle through the woods with his wife Sabine. The chemist also enjoys helping his son Adrian work on his model steam engine.

properties satisfy the requirements for initiation of a clinical study. The chemists must synthesize thousands of test compounds until getting it just right. Some 700 syntheses were required for rivaroxaban and approximately 2,000 for riociguat. Some of them came from Straub's laboratory. "It's fair to say that all of our chemists had a hand in creating riociguat," says Straub. Not until years later, however, did it become clear that rivaroxaban and riociguat had genuine potential for success.

"I'm going to be a chemist!" – in elementary school, Straub already knew what he wanted to be when he grew up.

Chemistry with effervescent powder and homemade rockets

While his schoolmates strived to emulate soccer stars from the VfB Stuttgart team or raced their matchbox cars, Straub invested his pocket money in chemicals and Erlenmeyer flasks, transforming his room into a chemical laboratory. He concocted baking powder and effervescent powder, and used the garden as a launching pad for homemade rockets. His parents, both artists from Stuttgart, were surprised by their son's "very different nature." Yet they encouraged him to go his own way and fostered his creativity, likely never suspecting what he was busy brewing up in his room. They even bore minor mishaps such as scorched furniture without complaint.

As the years went by, Straub's interest in the theoretical fundamentals of chemistry grew. He learned how to apply scientific working methods, successfully participating in contests for adolescent researchers. "I was something of a troublemaker in chemistry class, however, because I was so bored," he recalls. As a teenager, he was especially fascinated by biochemical and medical questions: "It was exciting to discover how diseases can be traced

back to biochemical processes and what reactions certain substances can trigger in the body," he says. He originally sought to study biochemistry, but was turned down because of a lack of study places. In retrospect, Straub feels this was actually a blessing in disguise. He loved preparative work in the field of organic chemistry and was delighted "when the crystals sparkled in flasks at the end of a synthesis." He retained an active interest in medicine and biochemistry, however. As part of his doctoral thesis, he researched the bioorganic synthesis of amino sugars, earning his degree *summa cum laude*.

In the late 1980s, this topic led him straight to his current employer. At that time, Bayer pharmaceutical researchers were examining similar molecules for development of the diabetes medication Glucobay®. One of Straub's former fellow students was part of the team. He helped arrange a temporary stay at the research center in Wuppertal for Straub. "I accepted the invitation and unexpectedly found myself in the middle of an application process," says Straub with a laugh. The company made an offer and Straub accepted, beginning his career at Bayer in 1989 as a lab head for cardiovascular research.

Thanks to his new colleagues, leaving Stuttgart proved easy. "It was a culture shock in a positive way," Straub



Need to experiment: even at primary school, Straub knew that he wanted to become a chemist and practiced with Erlenmeyer flasks and chemicals.

says with a smile. He liked the open-minded atmosphere, casual style and matter-of-fact interdisciplinary cooperation on the campus in Wuppertal. A positive development in his private life was soon to follow. Straub lived right next door to a young female laboratory assistant in the Bayer apartment house. The two soon became a couple. They married in 1996 and welcomed their son Adrian a year later. The Straubs have long since traded their company housing for a spacious apartment in an art nouveau villa. The family now has its new home in Wuppertal's green zoo district, just a short distance away from Straub's Medical Chemistry laboratory in the research center belonging to Bayer HealthCare.

Excursions into pesticides research expanded horizons

For a time, Straub had a longer trip to work. After eleven years in pharmaceutical research, Straub switched to Bayer CropScience in Monheim in 2000, where he was involved in process research and development. Here he became acquainted with additional steps in the path from active substance to commercial product. Safe, ecological and efficient processes are crucial when producing active substances by the ton. "The chemists here are total professionals. They optimize each procedure in minute detail." Straub was looking for a production procedure for the new fungicide bixafen. Since active substance costs play a decisive role in agriculture right from the start, the procedure had to make do with "homeopathic amounts" of an expensive catalyst. It was a change of perspective that taught him valuable lessons.

After seven years at Bayer CropScience, the full-blooded researcher returned to Wuppertal. Today, cardiology research is once again the focus of his work: "Cardiovascular diseases are one of the most common causes of death worldwide. There is still no adequate treatment for some of them, such as stroke and heart failure," says Straub

in describing the ambitious goals of his work and what motivates him. In order to solve the complex tasks he faces, Straub often uses the early evening hours, when quiet falls over the institute after the hectic working day. "That is when I am at my most creative, can process information and generate new ideas," he says.

Straub can rely on his experience in his research, but notes that: "If you want to risk doing something new, it is even more important to remain open-minded, to question apparent certainties and to always think outside the box." He adds, "Every researcher must also be open-minded enough to recognize when a project has failed." His optimistic attitude and sense of humor are a great help in such cases. Not merely a master of his trade, Straub is also a master of situational comedy who never fails to see the funny side of day-to-day life. The liberating power of laughter helps him stay calm, and both co-workers and staff appreciate his joie de vivre. So does his family, to whom his scant free time is devoted. At the weekend, the Straubs like to spend their time outdoors, cycling through the countryside of the Bergisches Land region or along the Rhine River.

Question apparent certainties – think outside the box

They also enjoy taking tours of various cities – especially when those cities have well-preserved art nouveau districts. Straub has a penchant for the architecture and design of the era: "If he discovers an unusual Tiffany lamp, he has to have it," says his wife Sabine. True to style, over twenty such lamps adorn the Straubs' spacious apartment in a historic building. The researcher is also fascinated by the natural sciences. Occasionally, he retires to the sofa alone after work with a book on great scientists. The next morning he is once again ready to devote himself to his latest cardiovascular research project – in search of surprises with targeted research methods.



Successful research: Dr. Alexander Straub (photo, top) is tireless in his search for new active ingredients – whether on his own or in a team, for example with Dr. Susanne Röhrig (photo, center). His achievements have been recognized with the Otto Bayer Medal, which he received together with (photo below, left to right) Dr. Frank Misselwitz, Dr. Susanne Röhrig, Dr. Klaus Wehling, Dr. Elisabeth Perzborn and Dr. Emanuel Lohmann in 2006 for Xarelto®.