

A pioneer in the service of patients

Chemist and pharmacologist Johannes-Peter Stasch has dedicated his scientific career at Bayer HealthCare to helping patients who suffer from conditions like pulmonary hypertension, for which no drug therapies were available for many years. His work has met with success: today "his" first drug is available on the market and several hundred researchers are working on the biochemical signaling cascade that first fascinated this Bayer scientist all those years ago.



The untiring researcher: Professor Johannes-Peter Stasch is not one to rest on his laurels and is continuing to work on new active ingredients.

Professor Johannes-Peter Stasch smiles as he recalls that “as a child, I was always asking Why not?” Even now, challenge clearly only motivates him even more. “Someone saying, ‘That’s impossible!’ always triggers a reaction in me,” he admits. This attitude has been good news for many patients, in particular for people with cardio-pulmonary diseases such as pulmonary hypertension, or chronic heart failure. “My research is for people suffering from severe illnesses for which no drug treatments previously existed,” Stasch explains. It’s what motivates him, and a cause he champions among his colleagues in the scientific world outside the Bayer organization as well. Stasch is not a medical doctor; he is a chemist and pharmacologist at Bayer HealthCare’s Global Drug Discovery department. He develops new pharmaceutical active substances, and only rarely comes into direct contact with patients. Nevertheless, the 60-year-old always has the people



Bayer scientists in debate: Dr. Dieter Neuser, Dr. Stephan Vettel and Professor Johannes-Peter Stasch (photo above right, left to right) discuss a model of the lung. Stasch spends lots of time working in his laboratory in Wuppertal with colleagues like Yvonne Keim, Andreas Hucke and Christina Jochem (photo above left, left to right), but also enjoys visiting Berlin (top photo).

he wants to help in mind. His passion for his subject knows no boundaries; he is renowned for working nights and weekends on their behalf. Stasch has more than 150 scientific articles on his publications list, including contributions to the prestigious research journal *Nature*. This industry researcher, who began his career at Bayer HealthCare 30 years ago, has earned the respect of the academic world for his achievements.

A scientist with innovative ideas and infectious enthusiasm for new medicines

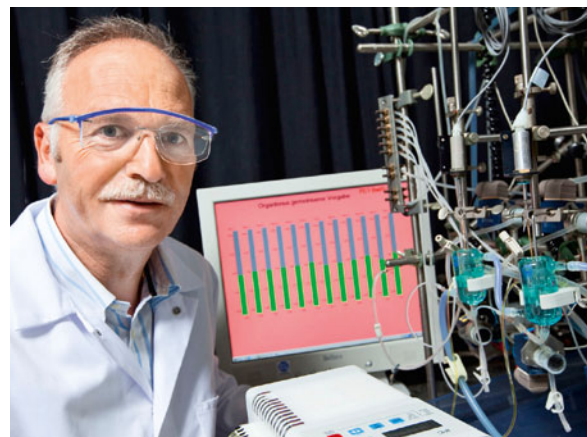
In 2010 he was named Honorary Professor of Drug Research by Halle-Wittenberg University. In 2013 he received one of the greatest honors bestowed on scientists in Germany by being elected a member of Leopoldina, the German National Academy of Sciences.

Stasch is not the kind of researcher who stays holed up in his laboratory behind a mountain of textbooks. He has a well-de-

served reputation as a lively and motivating speaker. “It’s important to sell your results, to go public and get others excited about them,” he says. Apart from his prolific writing, his inquisitive mind has led to more than 200 patent applications. When asked for particular memories, Stasch is quick to bring to mind one patient: a young woman suffering from pulmonary hypertension. In this severe, progressive disease, the walls of the pulmonary arteries thicken, becoming stiff and increasingly inflexible. The supply of oxygen to the bloodstream is decreased as a result, leading to a risk of heart failure. “This woman could hardly lead a normal life,” Stasch relates. “Even

The substance that dilates blood vessels

One of the active substances at Bayer is member of a class of vasodilators known as soluble guanylate cyclase (sGC) stimulators. Soluble guanylate cyclase is an enzyme that plays an important part in the cardiovascular system. It is activated by the nitrogen monoxide produced by the human body. Following activation, it stimulates production of a cellular messenger substance known as cyclic guanosine monophosphate or cGMP. This molecule in turn dilates the blood vessels. In many cardiovascular diseases, however, this signaling cascade does not function properly. In some cases, too little nitrogen monoxide is available, the sGC enzyme does not react adequately, and not enough cGMP is produced. The blood vessels constrict in response, such as in the case of pulmonary hypertension. This is where the sGC stimulator intervenes: it stimulates the enzyme to increase cGMP production even independently of the nitrogen monoxide (NO) messenger substance. See also "Acquisition" on page 5.



Expert in sGC stimulators: Professor Johannes-Peter Stasch investigated the signal molecules that dilate blood vessels.

the slightest exertion caused her heart to pound wildly. She was short of breath and constantly tired." But then she took part in a clinical study. The object of the study was an active substance in the class of sGC stimulators. During her participation in the study her health status improved. "She could climb stairs again, go to work and do the things she wanted to do. Her whole family benefited," says Stasch, with no attempt to hide how moving that moment must have been for him. As the full story of sGC modulation unfolded, through the tireless work of Bayer researchers, and the particular benefits materialized for patients with pulmonary hypertension, it became clear to Stasch: "Our work has paid off, and the active substance has a very good chance of being approved as a drug for treating this disease."

Elucidating, influencing and repairing the signaling cascades inside cells

It was an overwhelming moment: because the highpoint of any pharmacologist's career is the day a new active substance discovered by him is approved by the regulatory authorities. Only few ever get to enjoy such an achievement. Johannes-Peter Stasch puts it this way: "Discovering and developing a new pathway is rare but also very exciting. Very correctly, the review of a compound with a new mechanism of action is a painstaking exercise." He is therefore all the more pleased that he succeeded in decoding a signaling pathway – and with it a small part of the complex machinery inside the cell – and was even able to influence it.

It was a long and arduous journey that began in 1994. At Bayer's Research Center in Wuppertal, Professor Stasch and his colleagues had just discovered and synthesized the first sGC stimulators. These active substances were shown to trigger a

complicated signaling cascade inside cells that in the end causes the blood vessels to dilate. As a result, Stasch and his team felt they could be useful for a number of diseases, not only cardiovascular but also for kidney and liver disorders, and various forms of dementia, because all these conditions are associated with similar biochemical mechanisms.

In dialog with outstanding scientists and Nobel laureates worldwide

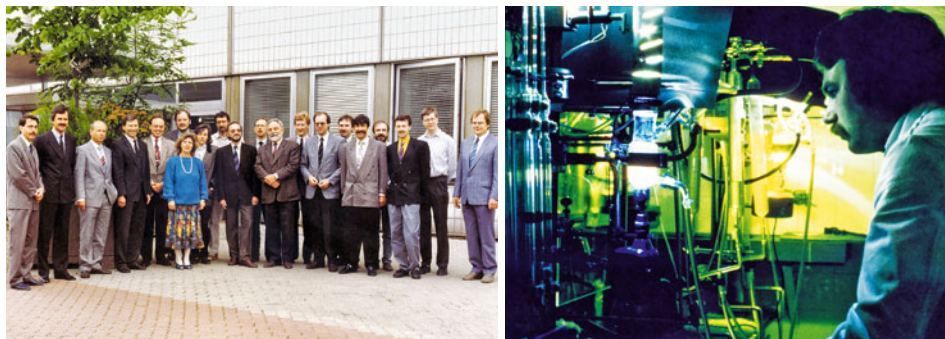
Unfortunately, research on sGC stimulators was always threatened by termination, because the substances, though promising, did not fulfill all requirements. Stasch repeatedly had to negotiate with management, get them interested in the potential of his work, even to the point of confrontation, "and show as much perseverance as I could muster."

From the very beginning, Stasch was committed to close collaboration with universities and research institutions. "The partnership between the industrial and academic worlds is beneficial to both," says Stasch, describing his view of modern research. In fact, the idea itself of searching specifically for sGC stimulators to treat pulmonary hypertension emerged from a collaboration with researchers at the Universities of Giessen and Harvard. Today Stasch has established a network of researchers around the world, including several Nobel prizewinners. "A lot of personal friendships have developed over the years from working together on the signaling pathway," Stasch says.

Anyone meeting the dedicated Bayer researcher immediately realizes that he treats everyone around him with the same candid friendliness. From the colleague who has just returned from an extended vacation, to the cleaning lady in the laboratory, he always has a friendly remark or quick joke to share with everyone. In his free time, he and his wife are involved in com-

Milestones in a researcher's career

Johannes-Peter Stasch (born in 1954) discovered his passion for chemistry at age 10, thanks to a chemistry set. After graduating from high school in Hameln, Germany, he majored in chemistry at the universities of Hanover and Würzburg. During his subsequent community service, he set up a neurochemical laboratory at Würzburg University Hospital. While working on his PhD, he completed his degree in pharmacy. In 1984 he became a licensed pharmacist and started his first job, working as laboratory director at the Institute for Cardiovascular Research at Bayer AG in Wuppertal. By 2008 he had risen to the position of Chief Scientist and become a member of the Bayer Expert Club, which advises the Bayer AG Board of Management on issues of innovation.



Images from the past: Stasch with his colleagues at the Pharmaceutical Institute in 1990 (photo left, 6th from right) and in 1978 at the Institute for Physical Chemistry at Würzburg University (photo right).

munity and social projects. Although he does not reveal more, it is apparent that the energy he exudes infects people in these pursuits just as much as in his scientific work. He even instilled his enthusiasm for science in his three children: they all grew up to be engineers.

With his untiring work, Stasch has established an entirely new field of research virtually from nothing over the last two decades. "Twenty years ago, it was just four of us sitting here at this table in my office," he recalls. Today several hundred researchers worldwide are investigating sGC stimulators and the messenger substance cGMP, which has a key function in the signaling cascade. In 2001 Stasch initiated a congress series on the subject cGMP, which he now organizes together with colleagues every two years. Today a lot of them know him only as "Mr. cGMP."

Skepticism as a motivator: Stasch counters critics with clear ideas and visions

Coworkers at Bayer also are intrigued by Stasch's achievements. "It is unbelievably impressive to see everything he has built up over the years," says for instance Dr. Peter Kolkhof, project manager in Cardiology Research at Bayer HealthCare in Wuppertal.

But Stasch himself is not one to rest on his laurels: "We are only at the very beginning of understanding sGC stimulators," he emphasizes, and sees a lot of work ahead. Stasch also wants to pave the way for another group of active substances, the sCG activators. These substances stimulate the same signaling cascade as sGC stimulators, but employ a different mechanism, activating the enzyme when it is altered by disease. For the sGC activators there is still a long way to go but thanks to the pioneering work of Stasch, the journey has begun!

Advising high-level policymakers

Professor Johannes-Peter Stasch was elected a member of Leopoldina in 2013. Germany's National Academy of Sciences is one of the oldest institutions of its kind worldwide. Leopoldina currently has some 1,500 members, all leading scientists from Germany, Austria, Switzerland and numerous other countries. The Academy's most important task is to advise policymakers: the members of its interdisciplinary expert groups draw up statements on key socio-political issues.



Elected to Leopoldina: Professor Johannes-Peter Stasch (8th from left) is a member of Germany's National Academy of Sciences.



www.research.bayer.com/stasch

Further information on this topic