PRESS RELEASE of the Boehringer Ingelheim Foundation – 14 October 2020

Targeting unwanted intracellular proteins for degradation
Craig M. Crews awarded the 2020 Heinrich Wieland Prize

Thanks to the results of his many years of research, Professor Craig M. Crews of Yale University in New Haven, Connecticut, is making innovative new medicines possible. So-called PROTACs (proteolysis-targeting chimeras) activate a cell's quality control system to target disease-causing proteins for degradation. These new active substances are intended to specifically destroy proteins that, until now, have been therapeutically impervious. For his ground-breaking research, Professor Crews has been awarded the 2020 Heinrich Wieland Prize.

Professor Crews will be presented to the public as the winner of the award, which is endowed with 100,000 euros by the Boehringer Ingelheim Foundation, during Berlin Science Week 2020. He will then speak as the guest of honour at *Starting up science: From lab to therapy*, a virtual event open to the public, on Monday, November 2, 2020, from 4 p.m. to 5 p.m. CET / 10 a.m. to 11 a.m. EST, about his experiences as a start-up entrepreneur in the field of science.

New pathways into cells
Deregulated proteins play an essential role in many diseases, from cancer and Alzheimer's to multiple sclerosis. Less than 20 per cent of all intracellular proteins can potentially be targeted by existing classes of active substances because they are catalytically active. The vast majority of all proteins are considered 'undruggable' or therapeutically impervious, as conventional active substances are only able to block a specific function of a protein if they can find an active binding site – something that most proteins do not offer. Through his research, Craig M. Crews is opening a new pathway. As early as 2001, he, along with Raymond Deshaies of the California Institute of Technology, first reported on PROTACs and their ability to dock onto any part of a harmful protein and thereby mark it for the proteasome, the cell's own protein shredder. However, it was not until 2015 that Crews was able to develop PROTACs that were small and stable enough to serve as potential drugs.

"By developing PROTACs, Craig M. Crews has created a completely new and fundamental concept for controlling the amount of any protein within a cell. This opens up great opportunities for many laboratories around the world, ranging from basic research of fundamental processes in cells to drug development," explains Professor F.-Ulrich Hartl, the chairman of the panel of independent scientists that selects the prize winners. Christoph Boehringer, Chairman of the Executive Committee of the Boehringer Ingelheim Foundation, adds: "Professor Crews' work spells hope for many people living with, for example, cancer or neurodegenerative diseases. It also shows how knowledge-oriented basic research can pave the way for new types of drug therapies."

Research results for medical practice
Professor Crews' scientific curiosity has always extended far beyond the boundaries of academia. Even his early research led to an FDA-approved drug for multiple myeloma. The basis of this drug was his discovery of how epoxomicin, a proteasome inhibitor, functions. He was also the first to synthesize epoxomicin in the laboratory.

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Professor Crews then founded Proteolix, his first company, and, based on his research, developed the proteasome inhibitor Kyprolis™. At Arvinas, a company he founded in 2013, Crews continues to develop the therapeutic possibilities of PROTACs. Initial clinical trials at Arvinas are focused on drugs that target androgen and oestrogen receptors in patients with metastatic prostate and breast cancer.

Event note
We would appreciate it if you could make editorial reference to the following event. Naturally, you are also cordially invited to attend as a media representative:

Monday, 2 November 2020, from 4 to 5 p.m. CET / 10 to 11 a.m. EST
Starting up science: From lab to therapy
with Prof. Craig M. Crews
A virtual event held as part of Berlin Science Week
www.heinrich-wieland-prize-2020.de

How does an idea move from curiosity-driven basic research to therapeutic reality? How do science-based start-ups succeed in the United States and Germany? These and other questions will be addressed in a livestream panel discussion and followed up with an open-floor discussion. The event's guest of honour will be Craig M. Crews, winner of the 2020 Heinrich Wieland Prize. The chemist and professor at Yale University is a pioneer in the field of controlled protein degradation. At the event, Professor Crews will exchange with scientists in Germany who, like him, have founded science-based start-ups. What were the basic conditions they required to found companies? What helped them and what didn't? In the second half of the event, the audience will be invited to participate in the discussion and contribute their experiences.

The participants in the discussion panel will be:

- Professor Craig M. Crews, winner of the 2020 Heinrich Wieland Prize, John C. Malone Professor of Molecular, Cellular, and Developmental Biology, and Professor of Chemistry, of Pharmacology, and of Management at Yale University, New Haven, Connecticut
- Professor Christian Hackenberger, Department Head at the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP) and Leibniz Humboldt Professor for Chemical Biology at Humboldt University, Berlin
- Professor Andrea Tüttenberg, Co-founder and CEO of ActiTrexx GmbH and Department Head of Skin and Lymph Node Sonography at the University Medical Centre of the Johannes Gutenberg University, Mainz

The event will be moderated by science journalist Monika Seynsche.

Craig M. Crews – Biography
Craig M. Crews is the most prominent pioneer in the field of targeted protein degradation. He is the John C. Malone Professor of Molecular, Cellular, and Developmental Biology, and Professor of Chemistry and Pharmacology at Yale University in New Haven, Connecticut. In 1986, he completed his undergraduate studies in chemistry at the University of Virginia in Charlottesville, Virginia, and subsequently did research at the University of Tübingen on a German Academic Exchange Service (DAAD) scholarship. In 1993, he received his PhD in biochemistry from Harvard University in Cambridge, Massachusetts. In 1995, he

moved to Yale University to become assistant professor of molecular, cellular and developmental biology, and in 2000 was promoted to associate professor. In 2003, he became the director of the Yale Center for Molecular Discovery. Professor Crews is a Fellow of the Royal Society of Chemistry and of the American Association for the Advancement of Science. In 2003, he founded Proteolix, his first company, and in 2013, he founded his second company, Arvinas, for which he is a scientific advisor. Professor Crews has received numerous awards and honours, including the 2013 CURE Entrepreneur of the Year Award, the 2014 Ehrlich Award for Medicinal Chemistry, the 2015 Yale Cancer Center Translational Research Prize, the 2015 Outstanding Investigator Award, and the 2017 AACR Award for Chemistry in Cancer Research.

About:

Heinrich Wieland Prize

This international award honours outstanding research on biologically active molecules and systems in the fields of chemistry, biochemistry, and physiology as well as their clinical importance. The 100,000-euro prize is named after the Nobel Laureate Heinrich Otto Wieland (1877–1957) and has been awarded annually since1964. Among the awardees – selected by a scientific Board of Trustees – are four later Nobel Laureates. Since 2011, the prize has been endowed by the Boehringer Ingelheim Foundation.
www.heinrich-wieland-prize.de

Boehringer Ingelheim Foundation

The Boehringer Ingelheim Foundation is an independent, non-profit organization committed to the promotion of the medical, biological, chemical, and pharmaceutical sciences. It was established in 1977 by Hubertus Liebrecht (1931–1991), a member of the shareholder family of the Boehringer Ingelheim company. With the Perspectives Programme Plus 3 and the Exploration Grants, the Foundation supports independent junior group leaders. It also endows the internationally renowned Heinrich Wieland Prize as well as awards for up-and-coming scientists. In addition, the Foundation is donating a total of 154 million euros from 2009 to 2027 to the University of Mainz to finance the scientific operations of the Institute of Molecular Biology (IMB). Since 2013, the Foundation has been providing a further 50 million euros for the development of the life sciences at the University of Mainz.
www.boehringer-ingelheim-stiftung.de/en/index.html

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