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## **FOR IMMEDIATE RELEASE**

### **The University of Massachusetts and Lundbeck Inc. Enter Research Collaboration to Explore Potential Targeted Therapy for Huntington's Disease**

*Expert team of scientists to study RNAi technology as a means to shut down production of a protein responsible for the disease*

January 27, 2011 – The University of Massachusetts Medical School (UMMS) and Lundbeck Inc. today announced a research collaboration aimed at further development of a targeted therapy to slow or halt the progression of Huntington's disease (HD). At this time, there is no way to stop or reverse the course of HD, a challenging hereditary neurodegenerative disease characterized by a triad of progressive motor, cognitive and emotional symptoms.<sup>1</sup> This collaboration will support a distinguished group of scientists in the study of RNAi-based therapies as a possible method for selectively suppressing production of mutant *huntingtin* (mHtt), the abnormal protein that causes HD.<sup>2</sup>

RNA interference, or RNAi, is a natural process that cells use to turn down, or silence, activity of specific genes. HD is mapped to a specific gene, which makes it a promising target for RNAi-based therapy because production of a mutant protein like mHtt can potentially be blocked by knocking down, or reducing, the gene's activity.<sup>3</sup>

"Our core idea is that RNAi can be used to selectively reduce mutant *huntingtin* production to slow or block the progression of HD, but we also hypothesize that excessive *huntingtin* silencing may impair neuronal function by interfering with essential signaling events," said **Neil Aronin, MD**, professor in medicine and cell biology at UMMS and principal investigator of the study. "This research collaboration allows us to test promising RNAi-based therapeutic vehicles to selectively knock down mutant *huntingtin* with the goal of restoring normal neuronal function. We've come a long way in pushing this research forward, and this next step with Lundbeck is extremely exciting."<sup>2</sup>

RNAi technology is used to interfere with the expression of a specific gene and, in this case, researchers will apply it to mHtt. This multi-faceted pre-clinical study progresses beyond previously successful mouse studies and could bring RNAi-based therapy one step closer to human clinical trials.

The study will evaluate potential dosing regimens of siRNA (small interfering RNA), packaged as short hairpin RNA (shRNA) and transported via the adeno-associated virus (AAV), a promising therapeutic vehicle for siRNA delivery to neurons. Additionally, researchers will work to establish the best brain distribution pattern for potential use of siRNA in clinical HD therapies. More specifically, a major element of the study will be to measure the volume of distribution in brain tissue of AAV-delivered shRNAmir (microRNA-adapted shRNA). This will permit researchers to evaluate the dosing of AAVshRNAmir in order to achieve spread throughout the striatum and nearby cortex.<sup>2</sup>

“We’ve followed Dr. Aronin and his team of researchers at the Medical School for some time and have been inspired by their bold exploration of RNAi technology and its potential use as a therapy for HD,” said Stevin Zorn, PhD, executive vice president, Lundbeck Research USA. “Lundbeck is proud to collaborate with such an exceptional group of scientists who are so devoted to those affected by this debilitating condition.”

In addition to Dr. Aronin, a talented group of scientists comprise the UMMS research team, including: Guangping Gao, PhD, who brings vast experience in developing adenoassociated virus; Richard Moser, MD, a neurosurgeon with expertise in resection of brain tumors and accessing brain compartments; and **Marian DiFiglia, PhD**, of Massachusetts General Hospital, an expert in the neuropathology and mechanisms of HD. Consultants on the project include: Kitty Clarence-Smith, MD, PhD, Lundbeck Inc., a neuro-pharmacologist who was instrumental in the approval process of the first FDA-approved drug for HD chorea; Robert Friedlander, MD, Professor and Chair of Neurosurgery, University of Pittsburgh School of Medicine, who has expertise in the study of neuronal survival in HD; and **Michael Levine, MD**, Professor and Chair of the Neuro-Psychiatric Institute at UCLA, an expert on HD animal models. The study is expected to be completed in 24 months.<sup>2</sup>

“During my years helping patients who are living with HD, our understanding of the disease has increased dramatically and opened doors for new approaches to treating the condition,” said **Anne Young, MD, PhD**, Chief of Neurology at Massachusetts General Hospital. “In my opinion, this approach hits the disease right at its core. If this method can reduce the huntingtin protein throughout the brain, it carries the potential to change the course of the disease.”

“The Hereditary Disease Foundation recognized the potential of RNA interference to cure Huntington’s disease when it was just being discovered,” says **Nancy Wexler, PhD**, President of the Hereditary Disease Foundation and Higgins Professor of Neuropsychology, Columbia University. “We organized the first Workshop in the world on this topic: ‘RNA Modalities in Huntington’s Disease Therapy,’ in 2002. The Workshop was led by Phillip Sharp, who won the Nobel Prize in 1993. This was the same year that our research team discovered the HD gene, a breakthrough that made gene silencing possible. Neil Aronin was a critical Workshop participant. The Hereditary Disease Foundation funded the very first research projects proving that RNA inference cures HD in mice. Silencing the abnormal protein gets at the heart of the problem. It is a unique and revolutionary approach to finding treatments.”

This collaboration is part of Lundbeck’s Huntington’s disease research initiative to identify and ultimately commercialize therapies that may slow or halt the progression of the disease. This research is driven by collaborations with academic institutions and companies with promising compounds in development. Those conducting early-stage HD research and interested in exploring opportunities to collaborate with Lundbeck should send an e-mail to [HDresearch@lundbeck.com](mailto:HDresearch@lundbeck.com).

### **About Huntington’s Disease**

Huntington’s disease is a hereditary neurodegenerative disease characterized by a triad of progressive motor, cognitive and emotional symptoms.<sup>1</sup> These symptoms vary from person to person. The survival time after the onset of symptoms can range from 10 to 30 years and currently there is no cure. It usually strikes in mid-life, although it can also attack children and the elderly. Each child of a parent with HD has a one in two chance of inheriting it. It has complete genetic penetrance, so that if someone inherits the HD gene, he or she will die of it.<sup>4</sup> The HD gene, whose mutation results in the disease, was localized in 1983 and isolated in 1993.<sup>5</sup> For more information on HD, please visit the Hereditary Disease Foundation website ([www.hdfoundation.org](http://www.hdfoundation.org)) and the HDSA website ([www.hdsa.org](http://www.hdsa.org)).

### **About the University of Massachusetts Medical School**

The University of Massachusetts Medical School, one of the fastest growing academic health centers in the country, has built a reputation as a world-class research institution, consistently producing noteworthy advances in clinical and basic research. The Medical School attracts more than \$255 million in research funding annually, 80 percent of which comes from federal funding sources. The work of UMMS researcher Craig Mello, PhD, an investigator of the prestigious Howard Hughes Medical Institution (HHMI), toward the discovery of RNA interferences was awarded the 2006 Nobel Prize in Physiology or Medicine and has spawned a new and promising field of research, the global impact of which may prove astounding. UMMS is the academic partner of UMass Memorial Health Care, the largest health care provider in Central Massachusetts. For more information, visit [www.umassmed.edu](http://www.umassmed.edu).

### **About Lundbeck Inc.**

Headquartered in Deerfield, Illinois, Lundbeck Inc., a wholly-owned subsidiary of H. Lundbeck A/S, is committed to providing innovative specialty therapies that fulfill unmet medical needs of people with central nervous system (CNS) disorders and rare diseases for which few, if any, effective treatments are available. For more information, please visit [www.lundbeckinc.com](http://www.lundbeckinc.com).

### **About Lundbeck**

H. Lundbeck A/S (LUN.CO, LUN DC, HLUKY) is an international pharmaceutical company highly committed to improving the quality of life for people suffering from central nervous system (CNS) disorders. For this purpose, Lundbeck is engaged in the research, development, production, marketing and sale of pharmaceuticals across the world. The company's products are targeted at disorders such as depression and anxiety, schizophrenia, insomnia, Huntington's, Alzheimer's and Parkinson's diseases.

Lundbeck was founded in 1915 by Hans Lundbeck in Copenhagen, Denmark. Today Lundbeck employs approximately 5,900 people worldwide. Lundbeck is one of the world's leading pharmaceutical companies working with CNS disorders. In 2009, the company's revenue was DKK 13.7 billion (approximately EUR 1.8 billion or USD 2.6 billion). For more information, please visit [www.lundbeck.com](http://www.lundbeck.com).

### **About the Hereditary Disease Foundation**

The Hereditary Disease Foundation is a publicly-supported organization focusing on finding treatments and cures for Huntington's disease. The HDF was founded in 1968 by Milton Wexler when his wife was diagnosed with the illness. The organization supports research to identify treatments and cures for Huntington's disease, including the development of mouse models, preclinical testing, studies of protein-protein interactions, strategies for gene therapy, intercellular signaling in striatal neurons and the development and planning of clinical trials.

The Hereditary Disease Foundation has the world's most prestigious Scientific Advisory Board focusing on curing Huntington's disease. The international Board of 30 scientists includes members of the National Academy of Sciences, the Institute of Medicine of the National Academy of Sciences, the American Academy of Arts and Sciences, Fellows of the American Association for the Advancement of Science, Fellows of the Royal College of Physicians, London, a Lasker Award winner, a Benjamin Franklin Medal in Life Science recipient and a Nobel laureate.

Scientific Advisory Board members include, among others, **Anne B. Young, MD, PhD**, Chief, Neurology Service, Massachusetts General Hospital, Julieanne Dorn Professor of Neurology, Harvard Medical School; **Marian DiFiglia, PhD**, Professor in Neurology, Massachusetts General Hospital, Harvard Medical School; **Neil Aronin, MD**, Professor of Medicine and Cell Biology, Department of Medicine and Graduate School of Biomedical Sciences, Chief, Division of Endocrinology and Metabolism, Co-Director, Neuro-therapeutics Institute, University of Massachusetts Medical School;

**Michael S. Levine, PhD**, Chair, Interdepartmental Neuroscience Ph.D. Program, Professor, Department of Psychiatry and Biobehavioral Sciences, Associate Director, Mental Retardation Research Center, Associate Director for Education, Brain Research Institute, Jane and Terry Semel Institute for Neuroscience and Human Behavior, David Geffen School of Medicine at UCLA; and **Beverly L. Davidson, PhD**, Roy J. Carver Professor in Internal Medicine, Professor in Neurology, and Physiology & Biophysics, Director, Gene Transfer Vector Core, Associate Director, The Iowa Center for Gene Therapy, Vice Chair for Research, Department of Internal Medicine, University of Iowa, *also a pioneer of gene silencing*.

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#### Sources

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