Jeffrey Conn

Researchers Strive to Refill Drug Discovery Pipeline

"There is a crying need for better drugs to treat people with serious brain disorders, such as schizophrenia, and for better ways to treat children with autism," said Jeffrey Conn, Ph.D., director of the Vanderbilt Center for Neuroscience Drug Discovery (VCNDD).

Vanderbilt is demonstrating how an academic medical center, in collaboration with corporate, foundation, and government partners, can "very clearly and deliberately deliver on a full pipeline of drug candidates," Conn said.

Vanderbilt is uniquely positioned to undertake early-stage drug discovery, in part because of its strength in clinical pharmacology, its investment in research infrastructure including high-throughput screening, its ability to attract government, foundation, and corporate support, and its recruitment of top-notch drug discovery scientists. The advances include the following:

Fragile X Syndrome

Researchers at Vanderbilt University Medical Center, in collaboration with Seaside Therapeutics in Cambridge, Mass., have achieved a milestone in the development of a potential new treatment for fragile X syndrome, the most common genetic cause of autism.

Drug-like molecules developed at Vanderbilt are undergoing the final pre-clinical studies required by the FDA before entering clinical testing at Seaside Therapeutics and could be ready for human testing in early 2012, said Jeffrey Conn, Ph.D., co-director of the Vanderbilt Center for Neuroscience Drug Discovery and a member of Seaside Therapeutics' advisory board.

Vanderbilt is also participating in clinical trials of another drug candidate developed by Seaside Therapeutics called STX209 (arbaclofen), which may decrease social withdrawal, a core symptom found in people with fragile X syndrome and autism spectrum disorders (ASD).

Fragile X syndrome, the most common inherited form of intellectual and developmental disabilities, is relatively rare, affecting approximately 90,000 people in the United States. Major symptoms include impaired cognitive function, developmental delay, attention deficit and hyperactivity, anxiety, obsessive-compulsive, and autistic behaviors.

Research conducted by the founders of Seaside Therapeutics and others suggest that excessive signaling through a receptor called mGluR5, which binds the neurotransmitter glutamate, may contribute to manifestations of fragile X syndrome.

In 2008, Seaside Therapeutics awarded Vanderbilt a $4.5 million grant to develop drug-like compounds that can improve fragile X symptoms by "tuning down" receptor activity. Last year, they began a second collaboration to discover and develop other classes of compounds that may be effective in treating the disorder. The National Institutes of Health also supported many of the studies that provided the groundwork for the Seaside-Vanderbilt collaboration.

Conn's colleagues in this effort included Craig Lindsley, Ph.D., co-director in the Center for Neuroscience Drug Discovery and director of medicinal chemistry; Carrie Jones, Ph.D., the center's director of in vivo pharmacology; Colleen Niswender, Ph.D., director of molecular pharmacology, J. Scott Daniels, director of drug metabolism and pharmacokinetics, Kyle Emmitte, Ph.D., research assistant professor of pharmacology and medicinal chemistry lead, and Alice Rodriguez, Ph.D., instructor in pharmacology.

Schizophrenia

Researchers at Vanderbilt University have identified chemical compounds that could lead to a major advance in the treatment of schizophrenia.

All current anti-psychotic medications act by binding to serotonin and dopamine receptors in the brain to help control hallucinations and delusions, but they provide little relief of other serious symptoms, including social withdrawal and the inability to pay attention or make decisions. As a result, many patients have difficulty holding a job or living independently. In addition, current drugs have serious side effects.

The new Vanderbilt compounds work in a fundamentally different way than existing medications, by inhibiting glycine transporter one (GlyT1), an action that allows for more normal function of brain cells involved in schizophrenia.

The novel compounds were developed by Jeffrey Conn, Ph.D., and Craig Lindsley, Ph.D., co-directors of the Vanderbilt Center for Neuroscience Drug Discovery (VCNDD), and their colleagues in the VCNDD, part of Vanderbilt University Medical Center.

Schizophrenia is a chronic disabling mental illness that affects more than 3 million Americans according to the National Institute of Mental Health, and 24 million people worldwide, according to the World Health Organization. The worldwide market for antipsychotic drugs exceeds $20 billion a year.

The Vanderbilt GlyT1 inhibitors were discovered and developed with support from the National

Institute of Mental Health. In 2010 the NIMH awarded Vanderbilt a five-year, $10 million grant to establish a National Cooperative Drug Discovery and Development Group, targeting new schizophrenia therapies.

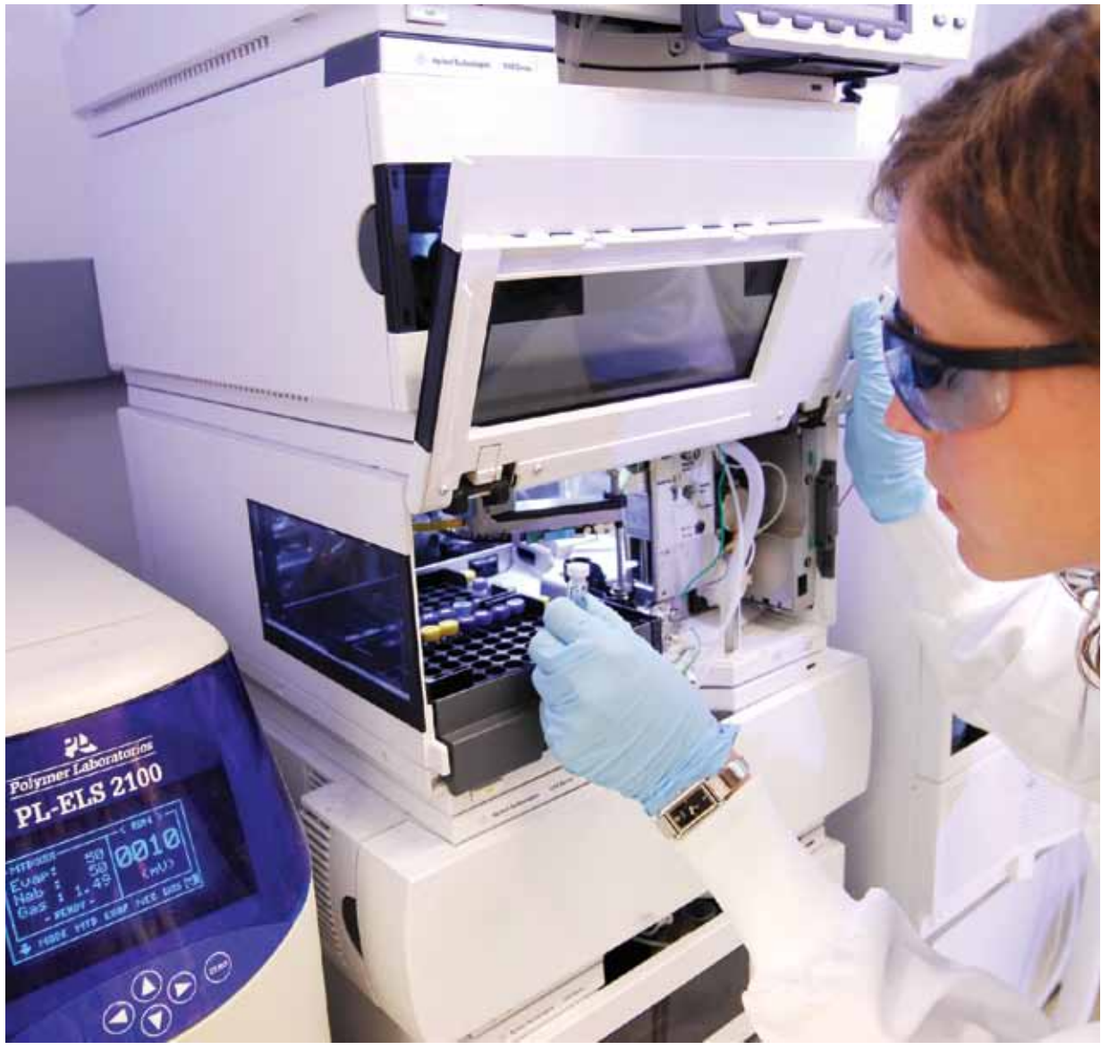
The work has been handed off to Karuna Pharmaceuticals, a Boston-based company focused on developing breakthrough therapies for schizophrenia, to which Vanderbilt has licensed its compounds.

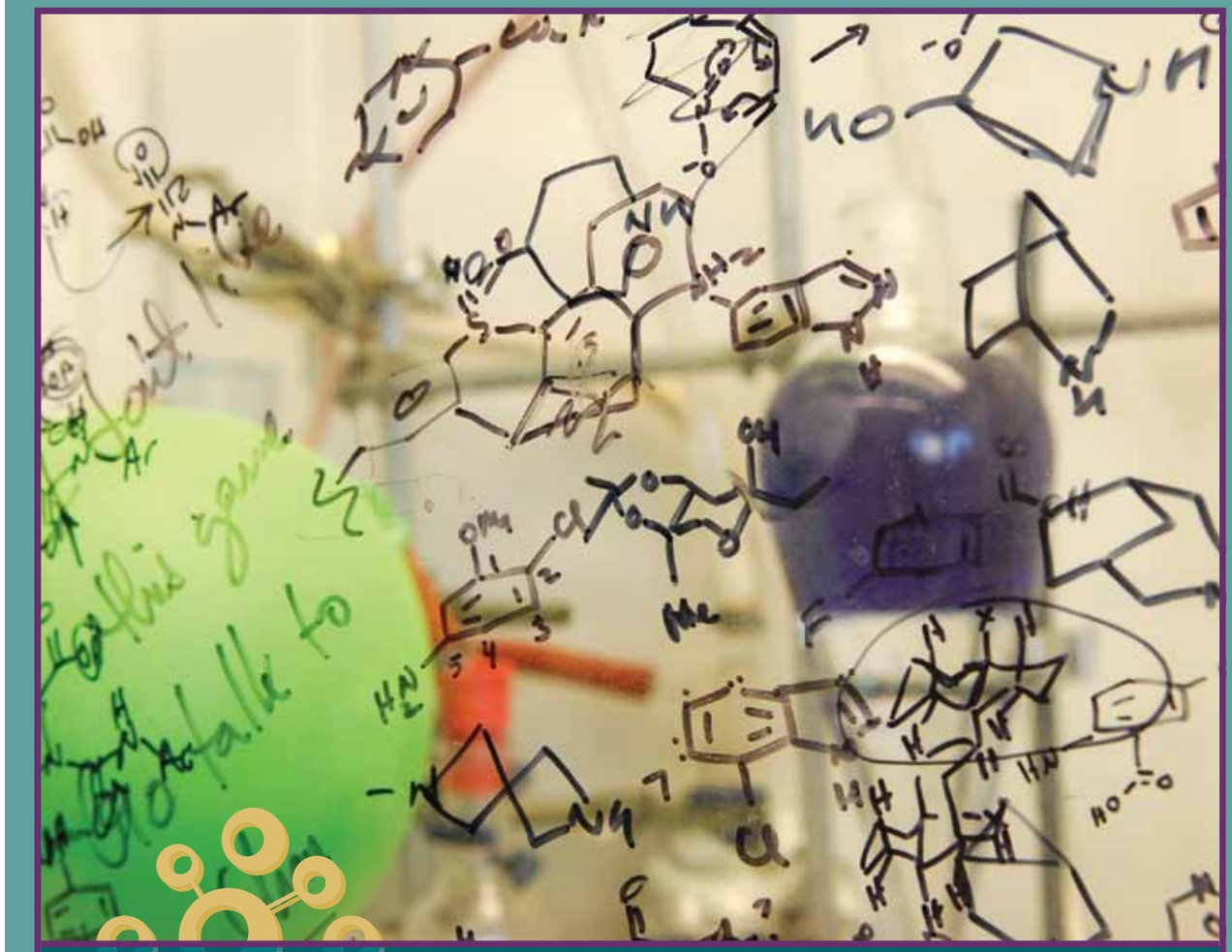
Conn and Lindsley's colleagues in the VCNDD on the schizophrenia program include Carrie Jones, Ph.D., the center's director of in vivo pharmacology; Colleen Niswender, Ph.D., director of molecular pharmacology; and J. Scott Daniels, Ph.D., director of drug metabolism and pharmacokinetics.

CTTC's Role

CTTC plays an essential role in helping VCNDD partner with industry to commercialize their research. The mission of VCNDD is to pursue advances in the understanding of human disease and drug targets in order to positively impact patient care. CTTC supports this mission and has been integrated into their leadership team to ensure that this goal can be reached.

The center manages all of VCNDD's intellectual property by protecting, marketing, and licensing the technologies they develop. The licensing staff actively seek industrial partners for VCNDD programs, facilitates funding agreements and licenses, and manages collaborations throughout their lifetime. CTTC worked with both Seaside and Janssen to design and customize agreements that would not only meet the goals of VCNDD and the scientific projects, but also be acceptable for each individual company. Both the Seaside and Janssen agreements are unique cases that have served as a model for many other academic and industrial partnerships.





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