**Science in Service to Humanity**

Norbert L. Wiech’s passion is saving lives. Quite a lofty goal by any standard, as Wiech, a 1960 graduate of Notre Dame, freely admits—but a goal the 66-year-old pharmaceutical entrepreneur feels is within reach, thanks to his collaboration with several scientists at Notre Dame’s College of Science.

Wiech, who received his doctorate in biochemistry from Tulane University, develops drugs—more specifically, “orphan drugs,” or treatments for rare diseases that large pharmaceutical companies have little interest in pursuing, as profit margins on their development are low. Says Wiech,“More than 6,000 rare diseases have been identified and, taken collectively, the number of people affected by those rare diseases is greater than those affected by heart disease and cancer. Out of those 6,000 rare diseases, treatments for only 300 have been approved by the FDA. Rare diseases don’t fit in with the business models of most large pharmaceutical companies.”

An orphan drug, as defined by the Orphan Drug Act passed by Congress in 1982, is intended to treat a condition that affects fewer than 200,000 persons in the United States. Individuals with rare diseases such as Niemann-Pick, Huntington’s, ALS (Lou Gehrig’s disease), sickle cell anemia, and thalassemia had little hope of a cure because patient populations were too small to encourage product development. Congress found that drugs for the treatment of more diseases would not be developed unless changes were made in applicable federal laws to provide financial incentives to develop such drugs.

The passing of the Orphan Drug Act encouraged Wiech, who has worked in the pharmaceutical industry for close to 40 years, to start his own small pharmaceutical company in Baltimore, Md. His first orphan drug—which successfully obtained FDA approval for medical use—was a therapy for UCD, or Urea Cycle Disorder, which had only about 240 identified patients in the U.S. Wiech was inspired in part, he says, because he saw the desperation of the families of patients with rare diseases. “When you have a child with a rare disease, the recognition that there is no treatment or cure is simply devastating,” he says.

His fervor to help patients afflicted with rare diseases and their families has fueled his research interests, but it wasn’t until a chance meeting in 1999 with Paul Helquist, professor of chemistry and biochemistry at Notre Dame, that he was able to move his research into high gear. Helquist introduced Wiech to Olaf Wiest, professor of chemistry and biochemistry, who specializes in computational organic chemistry. Wiech also was introduced to the work of Martin Tenniswood, whose laboratory focuses on developing treatments for prostate cancer, and to Holly Goodson, assistant professor of chemistry and biochemistry, who specializes in biochemistry and molecular biology.

Olaf Wiest and Norb Wiech

Wiech began collaborating with the Notre Dame scientists on the development of compounds called “HDAC inhibitors.” HDACs (histone deactylases) are one of the classes of enzymes in each cell that regulate which parts of the genetic code are expressed and produce the proper proteins. Inhibiting HDACs has evolved as a promising approach for the treatment

of different genetic diseases, as well as cancer.

Working together, the four scientists pooled their areas of expertise to design, synthesize, and assay several new types of HDAC inhibitors. Among the compounds that arose directly from their early computational modeling studies was CG1521. This compound was shown by Tenniswood to have a unique mode of action and utility for the treatment of prostate cancer. Since that time, several others have also been developed to provide what pharmaceutical companies call a “pipeline” of new compounds for future development. Helquist’s laboratory has continued to synthesize these new compounds designed by the Wiest group, which are then studied in the Goodson laboratory to confirm their usefulness. Finally, Helquist has also developed a greatly improved synthesis of trichostatin A, which is generally regarded as the “gold standard” of HDAC inhibitors. Wiech’s company, Errant Gene Therapeutics (EGT), is currently working with the researchers at the University to move these developments closer to the patients. Of immediate interest is the development of a treatment for sickle cell anemia.

All of this activity is geared toward developing treatments for rare diseases that would otherwise not be available. By combining their expertise in the areas of synthetic organic chemistry, computational molecular modeling, structural biology, biochemistry, cell biology, and molecular biology, this group of scientists and their colleagues in the College of Science endeavor to fulfill the mission of the University, which, simply stated, is to contribute to the common good. As Wiech says quite eloquently, “We subscribe to the concept put forth by Joe Marino, the dean of the College of Science, that through our activities and collaborations we are engaged in nothing less than pursuing ‘science in service to humanity.’”

**Sidebar: Transferring Technology to the Marketplace**

In 1931 Notre Dame had its first and most famous foray in technology transfer, when the groundbreaking work of Rev. Julius Nieuwland, C.S.C., with polymerized- 2-chloro-1,3-butadiene led to two patents and the development of the first synthetic rubber, Neoprene, by the E.I. DuPont de Nemours chemical company. That bit of “intellectual property” earned the University some $2 million by the time royalty payments ceased in 1948.

No other “invention” has brought so much recognition and revenue to the University, although some recent efforts are beginning to pay off, albeit modestly. While not in the same league as traditional powerhouses in technology transfer—such as the University of California system, Stanford, MIT, Johns Hopkins, and Wisconsin—the University signaled its support for the patent process by establishing the Office of Technology Transfer in 1999. The university has been issued a total of 55 patents, 11 of them since 1999, with 23 patents pending. And since 1999, license revenue has jumped from $342 to a cumulative $823,308 in fiscal 2005. Licenses have been granted to 13 companies to use technology developed at Notre Dame, and options are out to another four. In recent years four new companies have been formed to commercialize Notre Dame technology. Two of these companies were started by Notre Dame faculty. Additionally, there are seven pending license agreements, two of which are with new Notre Dame faculty start-up companies.

To put this into perspective, the 10-campus University of California system (ranked number one in technology transfer according to the Association of University Technology Managers) in 2004 earned $74.3 million with 270 patents issued. But, says Mike Edwards, an assistant vice president in the graduate school who heads up Notre Dame’s technology transfer office, most schools are “more at Notre Dame’s level. Very few universities actually make money on technology transfer.”

Then why engage in the process at all? “Well,” says Olaf Wiest, who along with colleagues Tenniswood and Helquist, are in the process of licensing their HDAC inhibitor compound to Norb Wiech’s EGT, “we will not cure anybody by publishing a paper.” Jeffrey Kantor, vice president and dean of the Graduate School, echoes this sentiment, “The reasons we’re involved in technology transfer efforts go beyond merely revenue generation. The key thing is that it allows what’s going on in our laboratories to have an impact on peoples’ lives.” He also acknowledges that technology transfer can and does stimulate economic development, particularly in the areas surrounding universities.