

Kalamazoo Valley Museum  
230 North Rose Street  
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[kalamazoomuseum.org](http://kalamazoomuseum.org)

Texas Township Campus  
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Arcadia Commons Campus  
202 North Rose Street  
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### **American Chemical Society has Granted Prestigious National Historic Chemical Landmark Status to Kalamazoo Scientists**

(Kalamazoo, Mich.) The American Chemical Society (ACS) has granted prestigious National Historic Chemical Landmark status to the steroid chemistry achievements of Kalamazoo scientists who worked at The Upjohn Company during the years 1950-1990. "Each Landmark designation represents a pioneering achievement that has contributed to society and the chemical profession," said Alan Rocke, chair of the National Historic Chemical Landmarks (NHCL) Subcommittee. "Upjohn's research in steroid medicines is a prime example, because it enabled the firm to make low-cost, high-quality treatments for debilitating diseases like rheumatoid arthritis. The company's innovations also contributed to the launch of the biotech industry."

The ACS established the NHCL program in 1992, to enhance public appreciation for the contribution of chemical sciences to modern life. Under the NHCL program, ACS grants Landmark status to seminal achievements in the history of the chemical sciences and provides a record of these contributions to chemistry and society. To date, 85 Landmark designations have been granted.

"The field of chemistry has transformed our lives, from advancing medicine and industry to creating new products such as steroid medicines, penicillin, plastics and more," said Steve Seceast, Kalamazoo ACS Local Section 2018 Chairperson. "A public dedication event and other activities are being planned to commemorate the Landmark designation. Plans include a banquet May 16, 2019 honoring the steroid chemistry achievements, a chemistry symposium and a dedication ceremony on May 17, 2019 to place a commemorative bronze plaque on permanent display at the Kalamazoo Valley Museum," Seceast said.

These activities are a collaboration among the Kalamazoo ACS Local Section, the ACS NHCL Subcommittee, Apjohn Group LLC, Kalamazoo Valley Museum (KVM), Kalamazoo Valley Community College (KVCC), Western Michigan University (WMU), Kalamazoo College (K-College), Pfizer, Inc., Zoetis, Inc., and local sponsors.

Mention steroids today and many people think of performance-enhancement drugs. Mention steroids in 1949, however, and most people thought of the new major medical breakthrough that one class of steroids, the corticosteroids, could successfully treat debilitating inflammatory diseases like rheumatoid arthritis. The discovery that steroid compounds like cortisone and hydrocortisone were safe and effective medicines was welcome news to millions of people suffering from inflammatory diseases. Unfortunately, in 1949, those medicines were only available from natural extracts or very lengthy manufacturing processes, making them scarce and prohibitively expensive.

"To make large volumes of the new corticosteroid medicines available at a reasonable cost, The Upjohn Company in Kalamazoo committed to an unprecedented expansion of an already established background in steroid chemistry work in the late 1940s," said Donald R. Parfet, retired Upjohn officer and great grandson of Upjohn Company founder, William E. Upjohn. "In

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1950 the company started what became an on-going program of steroid chemistry innovation. The commercial production of beneficial corticosteroids and later general steroid medicines was provided to the world through a continuous string of chemical and microbiological discoveries and inventions by Kalamazoo scientists," he said.

The Upjohn Company was a pharmaceutical manufacturing firm founded in 1886 in Kalamazoo, Michigan by Dr. William E. Upjohn, an 1875 graduate of the University of Michigan medical school. The company was originally formed to make friable pills, which were specifically designed by Upjohn to be easily digested. These could be "reduced to a powder under the thumb," a strong marketing argument at the time.

Upjohn developed a process for the large-scale production of cortisone. The oxygen atom at the 11 position in the molecular structure of this steroid is an absolute requirement for biological activity. However, there are no known natural sources for starting materials that contain that feature. The only method for preparing this drug prior to 1952 was a lengthy synthesis starting from cholic acid isolated from bile. In 1952 Upjohn scientists Durey Peterson and Herbert Murray announced that their development team was able to introduce this crucial oxygen atom by fermentation of the steroid progesterone with a common mold of the genus *Rhizopus*. Over the next several years, chemists headed by John Hogg adapted this microbiological oxidation into a process for preparing cortisone from the sterol stigmasterol. Another key step, the efficient extraction of the minor stigmasterol from a waste stream of processing soybeans into purified oil, was engineered by J.Ward Greiner's team.

Following on the successful syntheses of cortisone and hydrocortisone, the steroid chemistry work was further advanced to produce improved, later-generation medicines like prednisone and prednisolone. These advances, which also improved the general science of chemical synthesis, include the well-known "Upjohn dihydroxylation" by V. VanRheenen, R. C. Kelly and D. Y. Cha in 1976. The industrial synthesis of corticosteroids was changed forever by multiple inventions in 1982-1990 enabling the use of the major component of soy sterols (sitosterol). Once again, microbiological steps (M.G. Wovcha, F.J. Antosz, J.C. Knight, C.B. Biggs) were combined with chemical innovations such as the Silicon Nucleophile Annelation Process (SNAP, D.A. Livingston, B.A. Pearlman and S.E. Denmark). The resulting corticosteroid active ingredients were formulated and analyzed by other Upjohn scientists into steroid medicines, and even sold to other companies worldwide for use in other medicines.

In 1995, Upjohn merged with Pharmacia AB, to form Pharmacia & Upjohn. In 2000, Pharmacia & Upjohn merged with Monsanto's pharmaceutical operations creating Pharmacia, Inc., and spun-out the agricultural chemical business into a new public entity under the name Monsanto. In 2003, Pfizer acquired Pharmacia. Pfizer has maintained the large Kalamazoo manufacturing site, which is today the single largest integrated chemical and pharmaceutical site in its portfolio. The Upjohn Company history of innovative research and development is often referenced by the strong pharmaceutical brands it created throughout its more than 100-year history. Many patients and physicians today continue to benefit from steroid medicines such as Solu-Medrol, Depo-Medrol, Solu-Cortef, Depo-Provera, and Cortaid, as well as other brands like Xanax, Halcion, Motrin, Lincocin, Cleocin, Micronase, Zyvox, Rogaine, and Kaopectate.

Today, society benefits from continuing innovations by Kalamazoo scientists not only at Pfizer but also at nearby companies, like Bridge Organics, Kalexsyn, Kalsec and many others, and local colleges such as K-College, KVCC and WMU.

"The Kalamazoo Valley Museum is proud to be able to offer a permanent home for the ACS National Historic Chemical Landmark plaque," said KVM Director Bill McElhone. "The museum,

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located in downtown Kalamazoo on Kalamazoo Valley's Arcadia Commons Campus, provides free general admission and is open to the public seven days a week. It houses more than 55,000 Kalamazoo-area artifacts. This historic designation, for one of Kalamazoo's most famous institutions and the ground-breaking work of its scientists, is an important part of the region's history," he said. The Kalamazoo Valley Museum is operated by Kalamazoo Valley Community College and is governed by its Board of Trustees.

For more information about the American Chemical Society and the Landmark program, visit [www.acs.org](http://www.acs.org) and [www.acs.org/landmarks](http://www.acs.org/landmarks). For a schedule of local events associated with the May 2019 activities visit, [www.kalamazooacs.org/events/](http://www.kalamazooacs.org/events/).