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Chirality a Hot Commodity For Fine Chemical Players - chiral molecules, single enantiomer drugs

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Rhodia Chirex, Dow and Cambrex beef up the toolbox.

SEVERAL CONTRACT manufacturing companies are stepping up their ability to serve a potentially lucrative market area: the development, manufacture and supply of novel chiral molecules. Companies such as Dow, Cambrex and Rhodia ChiRex are quickly forming alliances that will diversify their technology platforms and reinforce their ability to get their technology and products to the marketplace.

In 1999, chiral molecules accounted for about one-third of the worldwide market for final pharmaceutical actives, according to the Falls Church, Va.-based Technology Catalysts International. Single enantiomer drugs were valued at roughly \$115 billion in 1999 and are projected to grow to \$150 billion by 2003.

"What we've seen in the past is that the single enantiomer products have been growing at least two times as fast as the market as a whole," notes Sandra Erb, manager of chiral and fine chemicals consulting at Technology Catalysts.

As a result, contract manufacturers are teaming up with biotech and life science companies to add new techniques and distribution capabilities to their portfolios, allowing them to better serve the growing demands of the pharmaceutical industry.

"I think most of these companies are trying to put together as diverse a group of technologies as possible so they can meet the needs of the industry," says Ms. Erb. "These chiral technologies are one way for them to differentiate themselves and make themselves more attractive to the pharma industry."

Last week, Rhodia ChiRex, a wholly owned subsidiary of Rhodia, and Aldrich Chemical Company announced the latest alliance. Under the agreement, Rhodia ChiRex will take advantage of Aldrich's service and distribution network to bring their novel chiral building blocks to the marketplace.

"The idea was to seed the market and get some of the products we've made with these technologies out to the marketplace and to customers. Aldrich has a great catalogue and network and its own customer base to promote our technology and the products made with our chemistries," says Stuart Needleman, vice-president of business development at Rhodia ChiRex.

Rhodia ChiRex's primary chiral technology is its proprietary Jacobsen Hydrolytic Kinetic Resolution technology, in which readily available racemic, aliphatic primary epoxides are catalytically resolved into the corresponding single enantiomer epoxide or ring opened to the corresponding chiral diol. In July, the company made its first licensing agreement of the kinetic resolution technology to Daiso Co. Ltd. for the manufacture and production of chiral epichlorohydrin and chiral chloropropane diol.

EXPANDING TECHNOLOGY PORTFOLIOS

Some companies are adding technologies that will build up their chiral technology toolbox while simultaneously complementing existing manufacturing capabilities to bring new products to scale. In addition, by expanding the breadth of chiral technology offerings, companies hope potential customers can find the right option to meet their needs.

Cambrex Corporation recently made a \$3 million investment in Synthon Chiragenies Corporation as part of a four-year collaborative agreement to develop, manufacture and supply advanced chiral compounds for use in therapeutic drugs. The deal also secures Cambrex an equity ownership position in Synthon with warrants for additional ownership.

"It's really part of our continued efforts to reposition Cambrex to the pharmaceutical industry and touch it all along the drug development and discovery process," says Anne-Marie Hess, director of investor relations at Cambrex.

Synthon is experienced in the area of carbohydrate-based chiral technology, opening up the possibility for Cambrex to create a library of new compounds that can be used to screen new drug candidates. Carbohydrates possess multiple chiral centers, which can lead to the development of more complex molecules that are often near-drug compounds themselves. When joined with Cambrex's enzyme technology, it is also possible to generate classes of molecules that are not easily reached by either technology alone.

"There's a natural way to take a class of our proprietary enzymes with a class of their products and make even more chiral building blocks. This project has already been started," notes Ron Carroll, vice-president of technology at Cambrex.

Dow Chemical Company is also delving into the area of carbohydrate-based chiral chemistry. In early December, Dow aligned with Australia-based Alchemia Pty. Ltd. to develop manufacturing capabilities targeting carbohydrate-based pharmaceuticals and nutraceuticals.

Alchemia's primary focus is on developing synthetic techniques and combinatorial libraries that can exploit the diversity that can be derived from carbohydrates and oligosaccharides.

"We're teaming up their synthetic capabilities with our process development techniques," says Mike Fazio, scientist at Dow Contract Manufacturing Services. "So as oligosaccharide or carbohydrate molecules that are identified need to be produced, together we can provide a solution and supply these chiral molecules to our customers."

In the future, Dow will look for opportunities to take advantage of overlaps in its enzyme capabilities and Alchemia's carbohydrate-based technology to develop novel chiral molecules.

Dow also recently teamed up with Diversa to jointly market capabilities for developing and producing chiral compounds of interest to pharmaceutical companies. Diversa will contribute its proprietary high-throughput technologies to identify and develop enzymes that can be used as bio catalysts in the development of pure chiral compounds. Prior to the Diversa alliance, Dow had enzyme screening capability and fermentation experience, but was not developing new enzymes.

"From a technical point of view, they bring high-throughput techniques of developing and screening new enzymes from unusual sources and they offer us a reduced timeframe in which we can develop enzymes for specific applications," says Cynthia Rand, scientist at Dow CMS.

The pharmaceutical industry is currently the primary channel for single-enantiomer products. The trend toward chiral drugs and intermediates has risen out of the search for safer and more effective therapies. Researchers found that in some pairs of racemates, one enantiomer is responsible for the therapeutic benefits, while the other contributes the side effects.

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