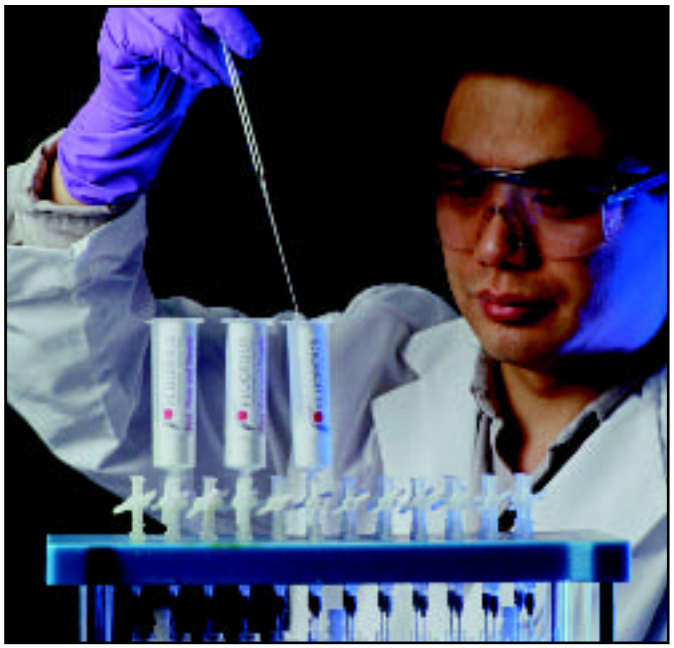
Applying fluorous chemistry in the medchem arena

Fluorous Technologies, Inc has greatly increased its technology offerings and expanded into new application areas in the drug discovery field in recent years. Company chief executive Philip Yeske explains his business strategy and looks at the potential of fluorous tagging for even further improving the identification of lead drug candidates.

Fluorous Technologies, Inc was spun out of the University of Pittsburgh Department of Chemistry in 2000 by the company's founder, Professor Dennis P. Curran. From the beginning, the company has been focused on the commercial utility of fluorous chemistry in the life sciences market.

Fluorous technology represents a chemical solution to separation problems, and is based on the highly selective and orthogonal nature of fluorine-fluorine affinity. The company's fluorous compounds contain a perfluoroalkyl group, or tag. Practically any organic molecule can have a fluorous-tagged form, which means that a wide range of syntheses can be adapted to employ fluorous separation technology. One of the major benefits of fluorous technology is its robustness and this applicability across a wide range of substrates allows diverse chemical compounds with very different chemical structures and containing a fluorous tag to be purified using a single chromatographic method. This saves a large amount of development time, which is of particular value in applications such as combichem and parallel synthesis, where procedures for the purification of new compounds are constantly required.

"Our business model has multiple revenue streams, from chemical reagent and sorbent sales to custom synthesis services," says company CEO, Philip Yeske. "We also pursue licensing agreements around the patents that protect our technology. Our early years have been focused on the small-molecule chemical discovery segment of the life sciences market, and we've made good progress with introducing our technology to that market in a challenging environment. The relative ease with which our technology can be implemented, without significant capital expense, has been a major reason for its promising adoption rate at a time when new technology evaluation is clearly a secondary priority."



An FTI chemist demonstrates parallel fluorous solid-phase extraction using a vacuum manifold.

MEET PHILIP YESKE OF FLUOROUS TECHNOLOGIES, INC

Dr Philip Yeske received a BS in Chemistry from Allegheny College in 1985 and a Doctorate in Organic Chemistry from Emory University in 1990. After working with Professor Dennis Curran (the future founder of Fluorous Technologies) at the University of Pittsburgh as a Postdoctoral Fellow, Dr Yeske joined Bayer Corporation in 1991. There he held positions progressing from basic research to global account management over a ten-year period, including a four-year assignment at Bayer's corporate headquarters in Leverkusen, Germany. In 2001 he joined Fluorous Technologies, Inc as the Chief Operating Officer and in February 2003 was promoted to President & Chief Executive Officer. Fluorous Technologies currently employs 14 people at its Pittsburgh, Pennsylvania, USA facility.

Demonstrating the value of technology

Yeske says that as a small business concern with limited resources, the company always faces the challenge of balancing focus with dexterity:

"By utilising government grants and outside collaborations, we've been able to demonstrate the value of our technology in several new market segments. These efforts are indeed an important investment in the future, as they could fundamentally change the strategic direction of the company.

"Fluorous technology is broadly enabling, and that opens up all sorts of possibilities for new areas of utilisation. We see excellent opportunities at the interface of chemistry and biology, and fortunately for us, that is the direction the life sciences marketplace is heading as well. We will continue to evaluate our facility, staff and capital needs as they relate to these opportunities," he says.

Application areas

The diverse range of fluorous chemistry tools available from FTI include affinity tags (protecting groups), synthesis reagents, protein and oligonucleotide purification tools, scavengers, peptide reagents and custom fluorous compounds.

An amazingly broad range of chemistries can be easily adapted to fluorous techniques.

Light fluorous compounds are soluble in organic solvents, and react according to solution-phase kinetics, which makes fluorous chemistry a good replacement for older solid-phase methods. An important example of this is scavenging: compared to solid-phase scavenging reactions, fluorous chemical reactions are cleaner, faster and more stoichiometrically efficient.

Biological molecules

The latest and fastest-growing application of fluorous technology is the purification of biological molecules such as peptides, proteins, oligonucleotides and oligosaccharides. In proteomics, fluorous affinity tags are used as a more selective, lower-cost alternative to biotin for the enrichment of natural polypeptides with low expression. In peptide synthesis, fluorous SPE is a general and simple way of achieving purities of 80 per cent or greater with the polarity of the peptide having little influence, thus greatly increasing the efficiency of a final HPLC purification. In oligonucleotide synthesis, fluorous-tagged phosphoramidites enable routine purification of sequences of 70 or more residues by fluorous SPE.

Fluorous HPLC can resolve fluorous-tagged compounds based on fluorine content.

FTI offers more than 200 fluorous chemistry products, one of the most important product families being fluorous protecting groups, which react like their more conventional counterparts such as Boc, TIPS, Cbz and Fmoc, but contain a fluorous tag that allows protected molecules to be manipulated using fluorous techniques.

The company also offers a wide range of fluorous reagents and catalysts. Excesses and by-products produced in reactions using fluorous reagents and catalysts are easily separated from non-fluorous products on completion of the reaction. A good example of this is Mitsunobu chemistry, in which all the by-products from the reagents are retained on the column during fluorous SPE, the required product flowing through in high purity.

For proteomics applications, FTI offers a range of fluorous affinity tagging compounds with chemical functionalities specific to various amino acids or post-translational modifications. The company also offers fluorous sorbents in a variety of formats for use with SPE, flash chromatography, TLC and HPLC in conjunction with all of the company's fluorous chemical products.

Performance prospects

"Our core business of reagent and sorbent sales into the drug discovery market continues to grow," says Yeske. "Short to medium term, we expect to further increase sales growth by penetrating faster-growing markets such as proteomics and biomolecule synthesis. Longer term, there are several high-value early-stage opportunities that are under exploration within the company that have the potential to redefine its direction.

"Our fluorous reagents for tagging and purifying small molecules are most critical to our business at this point in time, but it would not surprise me at all if the protein enrichment tags and biomolecule-focused technologies surpass them. Relative to chemical purification, there are far fewer tools on the market to effect simple, robust purification of biomolecules. This is a competitive advantage that we intend to fully exploit.

"I think that consolidation is inevitable as the pressure increases on large publicly traded organisations to identify and commercialise innovative technologies in order to drive profit margins. The appetite for growth is already strong and organic growth cannot possibly sustain it.

"Our vision for growth is strongly dependent on successful collaboration. Our doors are always open to anyone who sees an opportunity for mutual business success," he concludes. sp^2

FURTHER INFORMATION

Philip Yeske, PhD
Fluorous Technologies, Inc
970 William Pitt Way
Pittsburgh, PA 15238
USA
Tel: +1 412 826 3050
Fax: +1 412 826 3053

Internet Links: **Email: contact-fti@fluorous.com**
Web: www.fluorous.com

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