PEPTIDE SCREENING

ASSAYS A LA PHOTOLITHOGRAPHY

LONDON—A second round of financing for Affymax (Palo Alto, CA), the Netherlands Antilles-registered drug screening start-up, is due to be completed in June 1991. The move may raise not only capital (\$15-20 million) but also the company's credibility.

In late 1989, based largely on the reputation of its founder, Alejandro Zaffaroni, for starting successful companies in the pharmaceutical area (Syntex, Alza, and DNAX—all in Palo Alto, as well)—Affymax raised \$25 million. Much of it came from wealthy private individuals. Affymax is reticent about disclosing information on its current investors and would not comment on the suggestion from two informed and independent sources that the largest single investor is U.K. publisher Robert Maxwell.

The absence of established biotechnology investors has led to criticism that Affymax "took the path of least resistance" in its early financing. That looks likely to change in the second round. According to David Singer, the company's director of business development, its second-round investors are "blue-chip healthcare institutions from New York and similar European groups."

Although at its current rate of R&D burn Affymax will need further investment within the next two years, the president of the company's Pharma division, Leighton Read, is confident money will come through licensing agreements with major pharmaceutical companies. "Every major drug manufacturer has approached us because of the interest our drug-screening technology has stimulated. We are in the process of finalizing royalty and milestone agreements with a number of multinationals and will be making announcements later in 1991."

That sort of relationship would be a welcome reassurance to Affymax observers who, so far, have been interested in the company's "whiz-bang" technology and impressed by its management experience, but who believe that both the initial and current placements have highly overvalued the company.

The latest technology from Affymax is called VLSIPS—Very Large Scale Immobilized Polymer Synthesis. It combines photolithography and synthetic chemistry to enable a large series of derivatives of a polymer to be grown on adjacent areas of a surface.

As reported in a recent issue of *Science* (251:767-773), one of the ways VLSIPS can be used is as a multiple

peptide synthesis system. Amino acids protected with photosensitive chemical groups are anchored to an amino-activated glass slide. Illumination, which leads to deprotection, can then be applied selectively through the use of masking. New amino acids can then be added. The result, after several repetitions of masking, illumination, and synthesis—each taking three hours—is a square grid of 1,000-50,000 different peptides immobilized on an area of 1.6 cm². The peptides can then be screened for specific binding activities using fluorescently labeled antibodies or receptor fragments.

Read believes that VLSIPS takes screening for drugs into a new generation. "We talk about parallel processing in computing. Well, in screening, the previous state-of-the-art in parallel processing was the 96-well plate. With VLSIPS, we can put 10,000 separate syntheses on one centimeter squared." Read claims that VLSIPS will reduce the time frame of the early stages of drug development—parallel synthesis of analogs of a protoligand and initial evaluation—from months to days.

Not everyone is wholly enthusiastic about the potential for the Affymax

technology. Louis Nisbet, CEO of screening rival Xenova (Slough, U.K.) thinks VLSIPS is "either going to be the greatest thing since sliced bread, or is not going to live up to its promise. Until the method gives rise to good leads, the jury is still out." From Xenova's own work on the screening of fungal preparations, he notes that "only a very few compounds showing activity during screening are peptides. Most are heterocyclic or carbocyclic compounds."

Other, more independent, observers agree with Nisbet that the present peptides-only limitation of VLSIPS could be a weakness. "Nucleotides and carbohydrates will be important in the future." Affymax has done some work on oligonucleotide synthesis using VLSIPS and believes this may have applications as an anti-sense screening technique or as a confirmatory check on sequence information generated by the Human Genome Project.

If those applications pan out and if the pharmaceutical companies sign up and if the investor profile of the company firms up, then Affymax may be perceived from outside in a way that justifies Alex Zaffaroni's undoubted vision. —John Hodgson

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