

Drug Companies Join Forces In Search for AIDS Therapy

Although HIV is the most intensively studied virus in history, researchers haven't yet found a promising way to attack it—all the drugs tested so far against AIDS have grave drawbacks. Some have only limited effectiveness; others are highly toxic. What is more, the rapidly mutating virus can deftly sidestep even the more effective of these compounds over time. So most researchers are now hoping they can defeat the virus by bombarding it with several agents at once, a strategy they believe may increase the effectiveness of individual drugs, reduce toxicity, and prevent the virus from developing resistance as quickly as it otherwise would.

All well and good in theory, but how do you find the right combination of therapeutic agents when most of the drugs are made by different companies—and the pharmaceutical makers have traditionally been secretive about products in development? One obvious answer is for companies to share data and collaborate in testing specific combinations of drugs. But until recently, such collaborations in the fiercely competitive pharmaceutical business have been the exception. No more. On 19 April, 15 drug companies* from the United States and Europe announced that they have formed a pathbreaking collaborative agreement to speed the search for anti-HIV therapies.

Spearheaded by P. Roy Vagelos, chief executive officer of Merck & Co., the Inter-Company Collaboration for AIDS Drug Development aims to foster a "new synergy" among pharmaceutical makers through sharing of information and experimental compounds shortly after completion of "phase one" safety tests in small numbers of infected people. "The sooner we learn about other people's compounds that are safe and effective, the sooner we'll want to do combination trials with them," says Vagelos, noting

that companies will share preclinical toxicity data, too. Collaborating companies plan to standardize their assays so that data from different studies can be compared. There are limits, however, to this new spirit of cooperation: No commercial ties are to be formed, and companies will continue to pursue independent research and development.

People with experience in the drug industry say this opening of data books is unique. "The notion of sharing early results, particularly nonclinical results, is unheard of," says Allan Weinstein, a vice president of research at Eli Lilly and Co., one of the 15 collaborators. "This is a breath of fresh air."

Although some AIDS activists and drug company officials have reservations about the collaboration, most researchers are welcoming it. "It could be really helpful," says Anthony Fauci, head of the National Institute

of Allergy and Infectious Diseases (NIAID). "We have a bear of a time getting combination trials going." Dan Hoth, who heads NIAID's Division of AIDS, is equally optimistic. "If all of these companies are willing to share information about what they're doing in phase one trials and what they're getting out of

them, that could speed things up significantly," says Hoth.

Retrovirologist David Baltimore, the Nobel laureate from Rockefeller University who has been calling for an all-out AIDS research effort similar to the "Manhattan Project" that created the atomic bomb (*Science*, 19 February, p. 1112) is elated. "It offers real hope for AIDS patients," Baltimore says. He is particularly heartened by the prospect that companies might resurrect drugs for combination trials that have failed when used individually.

AIDS activist Larry Kramer stresses that this collaboration, though "gutsy and courageous," is not a Manhattan Project for AIDS, an idea he, too, has strongly promoted. "A Manhattan Project is much more basic science and requires a lot of money that no one's willing to lay out," says Kramer. "The symbolism of this collaboration is the enormous frustration that people like Vagelos feel—he's been very frustrated that Merck

hasn't been able to do more. This is really just a cry for help."

Kramer isn't the only one whose enthusiasm for the collaboration remains temperate. Though the 15 companies who signed on include most major pharmaceutical houses developing AIDS drugs, a few are conspicuously absent: Abbott Laboratories, Johnson & Johnson, Sandoz, The Upjohn Co., and Warner-Lambert. Upjohn says it didn't sign on because it already has a handful of anti-HIV drugs in the pipeline. "Every combination we can think of that we want to do, we have those drugs," says Jerry Mitchell, president of Upjohn Laboratories. "And there aren't any out there that look as good as ours."

Even some companies that agreed to the consortium had cold feet, which is why it took Vagelos and Edward Scolnick, president of Merck Research Laboratories, more than a year of backroom persuasion to firm up the deal. A chief concern has been anti-trust violations, but Vagelos says several attorneys agree that because the collaboration is not a commercial venture—no profits or marketing rights will be shared—those laws do not apply. Some companies also are nervous about treating AIDS differently from other pressing diseases. Vagelos and Scolnick emphasized that AIDS is different. "It's an emergency spreading around the world, it's caused by a known agent, and there are targets that have been identified," says Vagelos.

David Barry, a senior vice president at Burroughs Wellcome, which makes the biggest-selling anti-HIV drug, AZT, only signed on after he was assured the collaboration would not duplicate trials being run by NIAID. Barry also is uncertain whether Burroughs stands to gain from the collaboration. "We have access to a lot of phase one data already," says Barry, who believes the companies that will gain the most are those with the least experience.

But Vagelos says others will be surprised to learn what is in the works at Merck, a \$9 billion-a-year outfit that spends more on AIDS research than any other project. "People don't know what we have," says Vagelos. "We're secretive....Now they're going to know everything."

Details of how the collaboration will actually operate are still fuzzy—no one, for example, knows who will run the trials—and should soon be worked out by a committee of company representatives. "If we don't have anything going in 6 or 9 months, we'd be very embarrassed," says John Doorley, a Merck spokesman. But whatever comes of the collaboration, the willingness to share in a highly secretive industry indicates that the pharmaceutical companies now recognize that the existence of AIDS makes policies based on business as usual not quite good enough.

—Jon Cohen

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*AB Astra, Boehringer Ingelheim Corp., Burroughs Wellcome Co., The DuPont Merck Pharmaceutical Co., Eli Lilly and Co., Glaxo Inc., Hoechst AG, Hoffmann-La Roche Inc., Merck & Co., Miles Inc., Pfizer Inc., Sigma Tau, SmithKline Beecham, Syntex Corp.