MONEY MATTERS

The Marketplace of HIV/AID$

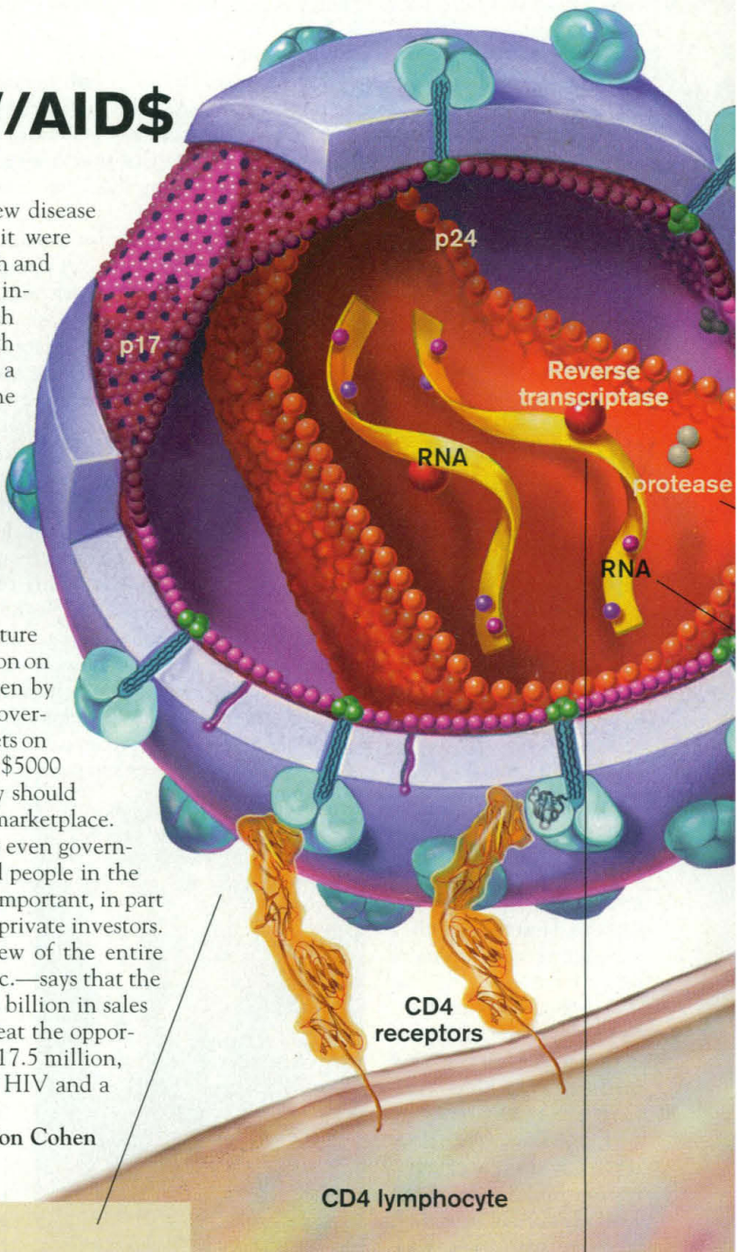
Thirteen years ago, when the public was just learning about a new disease called AIDS, the scientists tracking down the virus that causes it were already thinking about how their research could be marketed. French and American groups eventually claimed to have "co-discovered" HIV independently and in different ways. But in one respect their approach was the same: Shortly before announcing their discoveries, both rushed to file patents that described how to determine whether a person's blood harbored the virus. And thus they gave birth to the HIV/AIDS industry.

Today, the U.S. Patent and Trademark Office has awarded more than 1500 patents related to HIV and AIDS, and the Food and Drug Administration (FDA) has approved eight anti-HIV drugs, with a ninth in the wings. Companies are making millions of dollars on tests that screen blood for evidence of HIV and immune-system damage. And, while a few companies are interested in developing an AIDS vaccine, none has yet proved its worth.

Around this field of experimentation a vast body of business literature has grown up—an abundant, if not always reliable, source of information on the HIV/AIDS marketplace. Some of it consists of free reports written by Ph.D. or M.D. stockbrokers. Typically, these offer an HIV/AIDS 101 overview and, with little subtlety, attempt to persuade investors to place bets on this or that company. Other commissioned reports, which can sell for $5000 or more, aim to inform companies more objectively about how they should position themselves in the volatile and unpredictable HIV/AIDS marketplace. Even these vary in quality and reliability—not surprising, given that even government epidemiologists can't say whether the number of HIV-infected people in the United States is closer to 630,000 or 900,000. Still, these reports are important, in part because they inform the largest source of funding for AIDS research: private investors.

One comprehensive study, for example—a just-published review of the entire HIV/AIDS market sold by the financial analysts Frost & Sullivan Inc.—says that the industry targeted on HIV's nine genes and 17 proteins rang up $1.3 billion in sales last year. Just over half of that amount went to drugs designed to treat the opportunistic infections associated with AIDS. The rest of the money, $617.5 million, is linked to other parts of the virus, as shown in the illustration of HIV and a discussion of market forecasts below.

–Jon Cohen



Vaccines

The market for a preventive HIV vaccine is as murky as the related science. A half-dozen years ago, when analysts were heady about the prospects of vaccines made from genetically engineered versions of HIV's envelope protein, several ventured guesses about the potential market size. One optimistic 1989 report from Shearson Lehman Hutton projected that the 1993 market in the United States would be $974 million; more than half of that figure came from gay men, 4.5 million of whom supposedly would seek out the vaccine at a cost of $120 per series of shots.

Gross revenues in 1993, of course, totaled exactly zero. It is little wonder, then, that the buzzword about HIV vaccines today is "market failure," a phrase that means the capitalist incentive isn't high enough to meet the public health need. Indeed, few large companies are even interested in developing an AIDS vaccine (*Science*, 19 August 1994, p. 1028), for logical reasons. The size of the U.S. market is uncertain. Lawsuits are an ever-present threat in vaccine development. And, most critically, basic research has provided few strong leads as to what an AIDS vaccine should contain. As the Rockefeller Foundation's International AIDS Vaccine Initiative (IAVI) argued in a 17 August 1995 financial assessment: "In the current environment no one government or company has the resources or incentive to take on the challenge of developing an HIV vaccine alone." The IAVI report proposes a solution, though: Developing countries hard hit by the epidemic should join together and request a line of credit from an international aid agency, to create a "credible market" for a fixed-price vaccine. The needy must take the initiative, the report says, for "it is unrealistic to expect commercial vaccine companies to divert resources in favor of the development of a vaccine merely for the good of the public."

Reverse Transcriptase Inhibitors (RTIs)

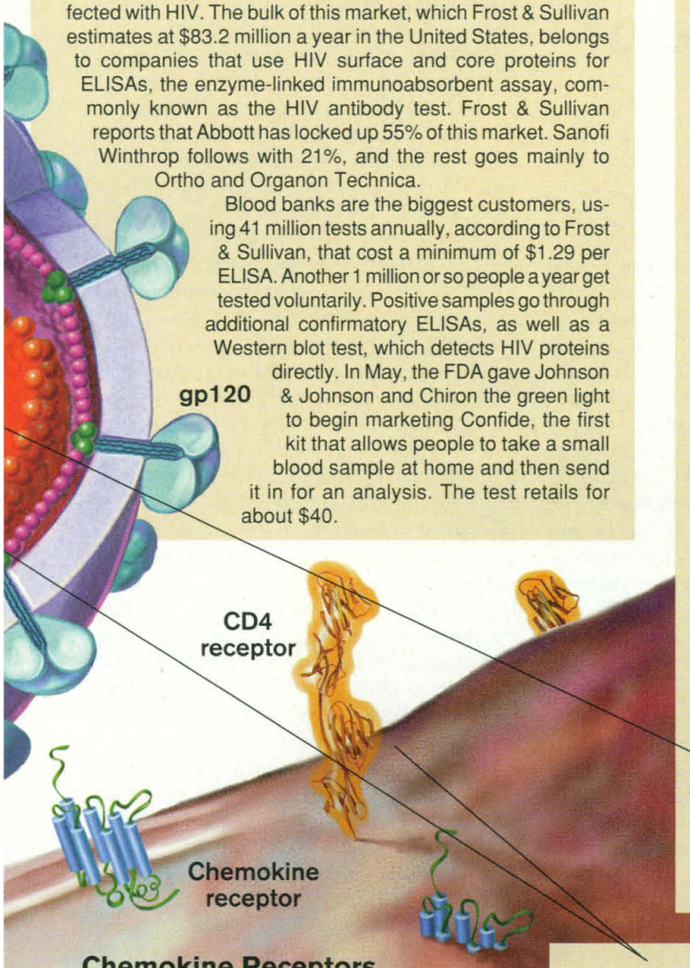
Five types of RTIs, the foundation of modern combination therapy, are now on the market. The granddaddy, AZT, was licensed in 1987 and still enjoys the largest revenue. AZT's manufacturer, Glaxo Wellcome, says the drug grossed $141 million in the United States last year and $317 million worldwide. Its cumulative worldwide sales to date: $2.5 billion.

Glaxo also owns licensing rights to BioChem Pharma's 3TC, an RTI that won approval last year because it appears to work synergistically with AZT. Between January and March 1996, 3TC brought in revenues of $39,932,000, according to IMS America, and it may ultimately rival AZT in sales. AZT, by comparison, sold $39,997,000 during the same period. Of the three other RTIs now

Diagnostics

Sexy new technologies are not yet appearing in diagnostics, the technology used to determine whether someone is infected with HIV. The bulk of this market, which Frost & Sullivan estimates at $83.2 million a year in the United States, belongs to companies that use HIV surface and core proteins for ELISAs, the enzyme-linked immunoabsorbent assay, commonly known as the HIV antibody test. Frost & Sullivan reports that Abbott has locked up 55% of this market. Sanofi Winthrop follows with 21%, and the rest goes mainly to Ortho and Organon Technica.

Blood banks are the biggest customers, using 41 million tests annually, according to Frost & Sullivan, that cost a minimum of $1.29 per ELISA. Another 1 million or so people a year get tested voluntarily. Positive samples go through additional confirmatory ELISAs, as well as a Western blot test, which detects HIV proteins directly. In May, the FDA gave Johnson & Johnson and Chiron the green light to begin marketing Confide, the first kit that allows people to take a small blood sample at home and then send it in for an analysis. The test retails for about $40.



Chemokine Receptors

The newly discovered link between HIV entry into cells and this family of receptors that bind to the anti-inflammatory chemokine molecules has already triggered late-night talks about who owns what. Smart money says there's gold in them thar hills.

on the market in the United States, IMS America data show that in 1995, the next-best seller was d4T from Bristol-Myers Squibb ($44.5 million), then Roche's ddc ($33.0 million), and Bristol's ddI ($19.6 million). On the horizon are nevirapine and delavirdine, members of a new class of RTIs.

Which of these drugs will dominate the market in the era of combination therapy is anyone's guess. Right now, many analysts seem giddy about impressive early clinical-trial results revealed this February for a combination of AZT, 3TC, and Merck's protease inhibitor. Analysts at Montgomery Securities, in fact, predict that by 2000, 3TC alone—which slows the development of resistance to AZT—will rake in $853 million in the United States. That's $100 million more than these same analysts forecast all of the protease inhibitors combined will gross that year.

Protease Inhibitors

The first drug of a new class aimed at stopping HIV by inhibiting its protease enzyme came on the market last December—Hoffmann-La Roche's saquinavir. Between December and March, according to IMS America—a Dun & Bradstreet company that tracks sales of drugs primarily through U.S. drug stores and hospitals—saquinavir had already grossed $35 million in revenues. This explosive early growth may slow a bit, as saquinavir now meets competition from protease inhibitors made by Merck and Abbott, both of which won FDA approval in record time this March (see p. 1882).

Many analysts have tried to assess where the protease market is headed. Their predictions are based on guesses about many variables: the number of people who will be infected with HIV, exhibit full-blown AIDS, seek treatment, or prefer one drug or a combination of drugs; how much they will pay for drugs; and whether they will develop drug resistance. Not surprisingly, the results are all over the map. "That really highlights the uncertainty in this marketplace," says Merck's vice president for anti-infectives, Bradley Sheares. Indeed, 3 years ago, no one would have predicted that combining AZT with 3TC would provide such a boost to their sales (see "Reverse Transcriptase Inhibitors," left).

One forecast, "The Protease Inhibitor Market," an 8 February report from San Francisco's Montgomery Securities, predicts that by the year 2000, 275,000 patients in the United States will be taking a mix of anti-HIV drugs. Montgomery also predicts that six protease inhibitors will be on the market then, each selling for $4000 a year, bringing in revenues of $755 million.

Another foresees a price drop, but larger total revenues. "Battling the HIV/AIDS Pandemic," issued on 23 August 1995 by Raymond James & Associates of St. Petersburg, Florida, predicts that in 2000, the annual per-patient cost of protease inhibitors will be about $2000. While this report does not predict the number of users, it suggests that the total "potential market" in the United States will be $1.18 billion. Like many others, this report builds on flawed data—in this case, even failing to subtract from projections the number of patients likely to die. Another problem that throws estimates off is the assumption that clinicians will be treating AIDS patients as their colleagues on the front lines of research do, but that won't happen. HIV Insight, a longitudinal database marketed by IMS America to track treatment patterns, shows that combination therapy—all the buzz among researchers—has been slow to enter the clinic. For example, 84% of the people who started to take anti-HIV drugs last year began with monotherapy. All forecasts are plagued by such flaws; industry insiders take them with a grain of salt.

Monitoring

A large and growing market—often overlooked—involves assays used by patients to track the disease and help make treatment decisions. According to Frost & Sullivan, this market reaped $92.3 million in revenues last year, two-thirds of which came from tests that measure levels of white blood cells with a receptor known as CD4, the docking point used by HIV's surface protein to infect cells. CD4 cell counts have become a bellwether for health status, because HIV selectively destroys them, giving an indication of how much damage has been done to the immune system. Frost & Sullivan analysts project that in 2000, CD4 tests alone will gross $128.4 million.

The rest of the monitoring market assesses the other side of the AIDS equation—how the virus is doing. A crude gauge of the pathogen's strength is a popular test that measures the viral protein p24. In clinical studies the p24 test has now been supplanted by more sensitive assays that measure levels of HIV's nucleic acid in plasma, recently shown to be powerful predictors of a person's disease course (*Science*, 9 February, p. 755). On 3 June, the first of these new "viral load" tests won FDA approval. Made by Roche Molecular Systems, this test uses the polymerase chain reaction to amplify HIV RNA. Already, competitors are preparing to enter the market. One of the strongest is likely to be one made by Chiron known as "branched DNA."

Mike Richey, Chiron's vice president of diagnostics sales, estimates that the potential U.S. and European market for all viral-load tests is $80 million to $120 million. His method of calculating the figure is revealing. Richey postulates that half of the HIV-infected people in the United States do not even know they have the virus. Of the other half, past sales of anti-HIV drugs reveal that, at most, 200,000 are being treated. Maybe another 50,000 are being seen by physicians. The rest know their status but are outside the health care system.

Richey assumes that the 250,000 people visiting clinics or physicians will each receive four viral-load tests a year—which would mirror the frequency of current CD4 tests. If each new test sold for $50 to $75, the current price of the Chiron kit, that would translate to revenues of $50 million to $75 million in the United States. The European market is thought to be about 60% as large.