PHARMACEUTICAL RESEARCH

Casualties Expected in Takeover Battle

LONDON—Ever since the British pharmaceutical giant Glaxo made a bid in late January to take over its smaller competitor Wellcome, with a promise to rationalize and streamline the operations of the two companies, scientists have been wondering how the merger would affect biomedical research. The answer, as outlined at a hearing held last week by the House of Commons Select Committee on Science and Technology, could be bad news for many researchers employed by the two companies but good news for academic scientists supported by the Wellcome Trust, Wellcome's biggest shareholder.

Following Glaxo's $13.9 billion bid (*Science*, 27 January, p. 443)—which Wellcome is trying to fend off—stock market analysts have estimated that the merger could result in joint cost savings of up to $1.6 billion annually, $600 million of which would come from R&D. An estimated 2100 research jobs could be lost in the United Kingdom, out of a total work force reduction of between 10,000 and 15,000. Glaxo Deputy Chairman and Chief Executive Richard Sykes did not want to discuss exact numbers, saying "it's a sensitive issue," but he told the committee "there will inevitably be job losses." He stressed, however, the potential for "big opportunities for jobs in the future," as the merged company would be able to invest in new technologies. "We're not interested in getting rid of good researchers," he added.

But Wellcome Chief Executive John Robb was more gloomy, saying his R&D work force would shrink and pointing out that "if there are less scientists ... it must be more difficult to bring more products to the market." Wellcome Research Director David Barry added that out of 80 products the two companies are currently developing, only two directly overlap—two anti-migraine compounds and two AIDS treatments—which provides little scope for eliminating duplication. He suggested that other research projects would inevitably be lost.

Both companies derive almost all their revenue from medicines and spend proportionally more on R&D—about 15% of total sales—than do other big pharmaceutical companies. Labour Member of Parliament (MP) Anne Campbell asked Sykes whether he could guarantee that the merged company's R&D spending would be a similarly high percentage. He said he could not, but maintained that the aim of the merger was to create a world-leading research center, with its base in the United Kingdom.

In written evidence, the Wellcome board argued that "it would be better for ... British science if another bidder were to emerge." That might yet happen, as Wellcome has been soliciting other offers and Robb referred to "some interesting meetings in the last few weeks." The results of the talks will not be known until the 8 March deadline for Wellcome's acceptance of the Glaxo offer.

The wild card in the pack is the Wellcome Trust, Britain's largest biomedical research charity, which owns 39.5% of Wellcome shares. The trust stands to gain $5.5 billion by selling its stake to Glaxo, a move it has favored from the start. The proceeds of the sale would yield interest of $78 million a year, Julian Jack, chair of the trust's scientific committee, told the MPs. "I have absolutely no doubt we will decide to invest that money in medical research. ... [It] would allow us to employ another 1000 scientists," he said.

One extreme indication of the anxiety generated by the takeover bid came last week when it was reported that one Wellcome trustee has been sent an anonymous threatening letter accompanied by a tube of unidentified white powder. The letter, apparently from a Wellcome employee, states that because the trust is willing to sell its Wellcome stock, "reprisals" will be necessary using "chemical, biological, radiological, and any other measures" against the trustees, their families, employees, and workplaces. A Wellcome Trust spokesperson says the matter is "in the hands of the police."

–Claire O'Brien

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AIDS RESEARCH

Glimmer of Hope for T Cell Booster?

The signature of AIDS is a steady decline in the number of white blood cells known as T cells. So it stands to reason that interleukin-2 (IL-2), a chemical messenger of the immune system that normally causes T cells to grow, might be a potent treatment for people infected with HIV. But, like most weapons deployed in the battle against AIDS, IL-2 failed to live up to expectations in clinical studies. And its brutal side effects have discouraged most AIDS researchers from pursuing it further. A group at the National Institute of Allergy and Infectious Diseases persisted, however, and this week it announced results from a small, long-term study that may revive hopes for IL-2.

In the 2 March issue of the *New England Journal of Medicine*, Clifford Lane, Joseph Kovacs, and their co-workers report that intermittent treatment with IL-2 can dramatically boost the number of CD4s, the very T cells that HIV targets and destroys. IL-2, the authors conclude, might help forestall HIV infection from turning into full-blown AIDS by "preventing the deterioration of the immune system to a level that renders patients susceptible to opportunistic infections."

Their optimism rests on 10 patients who had mean CD4 counts of about 450 per cubic millimeter of blood at the start of the study (600 to 1200 CD4s is normal), were on anti-HIV drugs, and did not have any opportunistic infections. After a year of treatment with IL-2, their mean CD4 count had jumped to 1000, with six of the 10 patients showing increases. A few of these patients even maintained their high CD4 counts for 1 year after the treatment ended. These numbers compare favorably with those seen in tests of anti-HIV drugs, where CD4 gains of 50 cells in a year are considered impressive.

Lane says the group's decision to treat patients intermittently—infusing them with IL-2 for 5 days every 8 weeks—may have been key to the results. The strategy may have given the immune system a crucial "rest" between doses, allowing CD4s to expand more robustly than they do when IL-2 is given continuously. "If [these changes] are more than anecdotal, they're very interesting," says the National Cancer Institute's Robert Gallo, whose lab discovered IL-2.

But Gallo and the authors both point out that the news is mixed. The IL-2 was costly—about $2500 for each 5-day infusion—the treatment required hospitalization, and it caused severe flulike symptoms and other side effects. And its success was patchy. In 13 of 15 sicker patients who had fewer than 200 CD4s at the trial's start, the IL-2 had no positive effect on CD4 counts and led to a higher level of HIV in their blood, which in itself could be harmful. Finally, this uncontrolled study did not gauge whether the treatment reduced disease and death.

Despite the mile-long list of caveats, Lane, Kovacs, and their colleagues are encouraged by their early results. They are now investigating whether they can make the treatment more "user friendly" by lowering the dose (and thus the toxicity) and switching to at-home subcutaneous injections. But the main question, stresses Kovacs, is: Does IL-2 delay or prevent AIDS? "The potential is there, but the proof is not." He and his colleagues are now conducting a controlled trial to see whether they can find that proof.

–Jon Cohen