

...but seeks 'practical' gene therapy deals

San Francisco. Despite a spate of discouraging clinical trials for experimental gene therapies, the interest shown by major pharmaceutical companies in the potential of gene-based medicine does not appear to be waning, according to biotechnology industry experts.

Just two weeks after separate groups of researchers reported that they had so far failed to treat cystic fibrosis and muscular dystrophy successfully with transplanted genes, for example, Hoechst Marion Roussel (HMR) announced a gene therapy agreement with Cell Genesys Inc. worth up to \$150 million, as well as two smaller deals, with the genomics companies Lynx and Incyte, worth a further \$50 million.

These were followed last week by various further announcements, including a \$25-million agreement between Rhône Poulenc Rorer (RPR), which is building up a network of agreements with various research groups in both the public and private sector, and AASTROM Biosciences Inc. for work on gene therapy techniques using lymphoid blood cells.

Executives in these companies remain optimistic about the potential of such alliances, and suggest that the gene therapy reports are unlikely to dampen their enthusiasm. Bob Pearson of RPR, for example, pointed out last week that "the drug industry is used to having failure for many years before eventually success, and it is going to be the same with biotechnology".

In an earlier statement, Jean-Pierre Godard, the global head of HMR, said that the deal in gene therapy for AIDS would place the company "at the forefront of the effort to commercialize emerging and novel

gene therapies".

According to analysts, however, the driving factor behind such investments is not the short-term prospects of rich profits from gene therapy, but the desire to build links with research groups that are able to produce practical clinical data about how disease genes operate. Whether or not they can produce gene-activated therapeutic techniques, small gene therapy companies are seen as a way of providing an efficient path to *in vivo* understanding of such processes.

"The [initial] clinical trials may be negative, but that's not scaring away prospective players, as that's not what they were looking for," said Mark Edwards, managing partner of Recombinant Capital, a consulting company in San Francisco.

Indeed, several major pharmaceutical companies have returned several times to their original partners to set up further joint projects. Baxter, for example, now has three separate agreements with Somatix Therapy, and Sandoz has three alliances with Genetic Therapy Inc.

At the same time, however, the dampening of initial euphoria has helped to introduce a new realism into these arrangements. Thus when Chiron took over the gene therapy company Viagene last month, it announced plans to lay off 20 per cent of the 160 positions at the San Diego company.

Chiron Viagene, the new subsidiary, is in the process of sharpening its focus on a narrower range of potential products, according to its president, Steven Mento. Viagene executives are being encouraged to look upon gene therapy as merely part of a toolbox that also includes small molecules and recombinant drugs. "Gene therapy doesn't

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New realism? Pharmaceutical companies are continuing to invest in gene-based research.

have to be the magic bullet," says Mento.

Part of the reason for general optimism among pharmaceutical companies is the recent loosening of regulatory requirements for gene therapy trials, and good news of other products in related areas. Linda Miller, an independent financial consultant in the life sciences based in Boston, suggests that their investments will now merely help to accelerate the development of gene therapy, but also benefit from a thinning of ranks of potential competitors.

Some major companies are still holding back from gene therapy as such. Executives with SmithKline Beecham, for example, say that, despite taking a significant stake in genomics through its \$125 million deal with Human Genome Sciences, and although such data are essential for the design of new drugs and diagnostic techniques, the applications to gene therapy remain uncertain.

Others, such as RPR, are continuing to develop strategies that rely on putting together a mix of experts to focus on specific diseases or gene delivery systems. "Companies are beginning to realize that gene therapy breaks down into a number of different elements, including tissue specificity, the targeting of delivery systems, and the regulation of gene expression, and that no one is going to lock into all of the science," says one leading investor.

At the same time, many researchers, perhaps sobered by the recent clinical setbacks in gene therapy, say that they are ready to redouble their efforts to understand the basic mechanisms that will underlie such techniques in future. "The areas of difficulty are clearly identified," says Inder Verma, of the Salk Institute in La Jolla, California. "Now it's just breaking the barriers."

Indeed, if the results of the clinical trials has damped public hype about gene therapy, this could be a good thing, says Verma. "The public should know the realities," he says. "Not everything is hunky-dory in this field."

Sally Lehrman

to biotech market as stocks recover

in London, suggesting that biotechnology has returned to favour in the market.

Addressing a meeting in London last week of investors in Biotechnology Investments Limits (BIL), a body set up by the late Lord Rothschild in 1981, Curnock Cook said that this optimism was reflected in a 27 per cent increase in the net asset value of BIL's investments — from US\$184 million to \$234 million — between the beginning of June and the end of August.

His analysis is confirmed by figures from investment advisers Piper Jaffray in Minneapolis, which show a sustained growth in the composite value of biotechnology stocks since the early summer, amounting to what the analysts describe as a 'positive trend reversal'.

Other data produced at last week's meeting showed that the recovery in biotechnology stocks has been led by some of the larger and better-known companies,

with 'top tier' companies such as Amgen, Chiron and Genesys all seeing their stock prices increase by more than 50 per cent in recent months.

According to Curnock Cook, one of the main reasons for the recovery has been a growing realization among small companies that the scientific skills required to get a new product into development are not necessarily the most appropriate for handling later stages in the development process, notably the broad-based clinical trials needed for regulatory approval.

Another factor said to have contributed to the recovery in biotechnology stock prices is the desire of investors to find new places in which to put money previously held in high-technology stocks. These have been among the fastest growing sectors of the stock market during the first six months of the year but may now, according to some analysts, be running out of steam. □