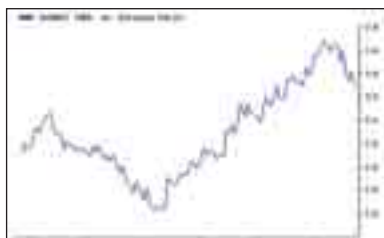


France's Exonhit greedy for take-overs

Appetite for Fusion

The drug discovery and diagnostics company Exonhit Therapeutics (Paris) has authorised an investment bank to search for take-over candidates, *Reuters* reported in June. Exonhit aims to enlarge its diagnostics business, seeking to become a mid-sized



Exonhit stock since December 2008.

company with sales of more than €100 million, the French company's Chairman, Loic Maurel, said, adding that, "the target company should be close to marketing a product but struggling for the means". Exonhit is also looking for partners for its two novel products related to Alzheimer's disease – one a blood test that can diagnose the neurodegenerative illness, the other a small molecule drug with neuroprotective properties that could possibly restore the cognition of sufferers to normal ("healthy") levels. Money shouldn't be a problem, given that Exonhit had €21 million in cash available at the end of 2008. On the other hand, the company suffered a €9 million net loss last year and revenue fell to a poor €4 million.



Exonhit's CEO Loic Maurel lustrates after fresh blood.

Exonhit was founded in October 1997. Its 70 employees use their knowledge about alternative RNA splicing to develop blood-based diagnostic tests and treatments for cancer and neurodegenerative diseases. Alternative splicing is a normal phenomenon in eukaryotes, where it increases the diversity of proteins (over 80% of genes are alternatively spliced). However, in certain cases, abnormal splicing variants are generated, leading to abnormal proteins that provoke a disease. Exonhit is able to identify many of these changes in splicing with its technology platform. In addition, the French use the genes encoding abnormal proteins as therapeutic targets for drugs. In the last 3 months, Exonhit's stock skyrocketed from €2.2 in March to €3.6 in June, pleasing its shareholders with a tasty 63% profit.

-WK-

Cancer drug Sutent disappoints

Universal Remedy Not So Universal

"More indications mean more profit." This is the simple but fruitful motto for a smart part of the pharmaceutical industry. Take a look at Sutent, a novel treatment for cancer, developed in the 1990s by a Max Planck Research group under German biochemist Axel Ullrich. After several company takeovers, the Sutent research project was finally completed by Pfizer in the USA. In 2006, the receptor tyrosine kinase inhibitor, that blocks cellular signaling related to tumor angiogenesis and tumor cell proliferation, was approved by the FDA for the treatment of kidney cancer and gastrointestinal tumors.

Thus, the small-molecule drug Sutent was the first cancer drug simultaneously approved for two different indications. A smash hit? Indeed, but not enough for Pfizer. Currently, the US drugmaker is testing Sutent for the treatment of many other cancers, such as lung cancer, colorectal cancer, liver cancer, prostate cancer and breast cancer.

Recently, however, Pfizer has had to say goodbye to a slice of the revenue cake. The pharmaceutical giant decided to halt a phase 3 trial of Sutent in advanced breast cancer after it had turned out that Sutent and the chemotherapy drug paclitaxel didn't offer better survival rates than the use of a combination of paclitaxel and Roche's cancer drug Avastin. This failure, however, doesn't matter. As a Pfizer spokesperson affirmed, the company will, "evaluate Sutent in advanced breast cancer through its two other Phase 3 clinical trials investigating the effectiveness of Sutent in combination with standard of care chemotherapies."

-WK-



No joke: US start-up raises €104(!) million

Urban Legend

It sounds like an urban myth: A well-rehearsed team of former biotech executives creates a company, with funds of – gasp! – not 1 million, not 5 million but a mere €104 million from venture funds (and many more millions to come).

However, this myth is true. The newborn start-up's name is Clovis Oncology Corporation, based in Boulder (USA), and the person behind the unusual venture is Patrick Mahaffy, a man who is well-known in the biotech industry. Mahaffy served as drug developer Pharmion's President and CEO from its inception in 1999 through its acquisition by Celgene Corporation eight years later. Mahaffy then pocketed a good portion of the takeover price's €2.1 billion and engaged the experienced former Pharmion team for his new child Clovis. The man knows a thing or two!



Clovis Oncology's Patrick Mahaffy doesn't intend to do things by half.



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With his proven team, Mahaffy intends to in-license a handful of promising early and mid-stage anti-cancer compounds, from developers without the money to advance their drugs themselves, and lead them to approval. "We won't do any discovery work ourselves," Mahaffy told the US web portal Fierce Biotech, "we focus on clinical development [incipient in Phase I or II] and managing the regulatory interface".

However, Mahaffy's skimming the cream won't provide many new jobs. He admitted that, "we don't require a large sales force or an army of people in clinical staff. We can work through CROs [Contract Research Organisations]. And we don't have to build discovery resources." Anyway, his Clovis Oncology Corporation will have, "a bright future in the cancer arena", Mahaffy believes. -WK-

Illumina cuts genome price in half

0,0011 Cents per Base

The proposed \$1,000 genome is still far away, but one big player recently made a decisive move to reach this holy benchmark. Illumina's Chief Executive, Jay Flatley, announced in June at the Consumer Genetics Show in Boston that his San Diego-based company will soon offer a €34,000 personal genome sequencing service. This price would obviously undercut the only other commercial personal genome service to date, offered by Knome. This Cambridge, Massachusetts-based company, that, "has been responsible for sequencing the genome of more humans than any company in the world" (according to Knome's own statement), banks €70,000 for whole genome sequencing. However, Knome promises to deliver detailed counselling and interpretation, while Illumina will not provide interpretation of data but delivers 30x coverage, employing paired end reads, SNPs and structural variation.

"We'll give not the genetic level look," Flatley said. "It's not Illumina's intent to connect genetic information to medically relevant information." The latter will be the task of other companies, he added, such as Navagenics and 23-and-me. -WK-

Roche celebrates 454th Genome Sequencer publication

Magic Milestone Reached

Just 4 years after the very first paper about next generation sequencing was published, a magic milestone has been reached. Roche Diagnostics recently announced that their 454th peer reviewed publication using the 454 Genome Sequencer System, has been released in *Nature Biotechnology* (a study by J. Kim and David Bartel, analyzing the influence of SNiPs on miRNA-mediated repression).

In September 2005, a *Nature* paper entitled, "Genome Sequencing in microfabricated high-density picolitre reactors," made plain to the scientific community that the times of Sanger sequencing will soon be over. Using a pyrosequencing protocol optimised for solid support and picolitre-scale volumes, a 56-person team, led by Marcel Margulies and Jonathan Rothberg, shotgun sequenced and *de novo* assembled the *Mycoplasma genitalium* genome with 96% coverage at 99.96% accuracy in one four-hour run. It was the starting point for an avalanche of hundreds more genome papers, using this new sequencing technique. The then state-of-the-art capillary electrophoresis sequencers, such as the Abi 3730xl, haven't been ditched altogether, but are side-



Large parts of the Neanderthal (left) genome have been reconstructed and compared to those of modern humans (right), using 454 sequencing technology.

lined more and more frequently to niche applications.

Roche's 454 Genome Sequencer was a forerunner for a band of next generation machines (Genome Analyzer by Illumina, SOLiD by Applied Biosystems, and others) that brought genome data to light at a speed that had been thought impossible before. In November 2006, for example, Svante Paabo announced in *Nature* that his team had deciphered the first million base pairs of the Neanderthal genome, aiming to complete the prehistoric human's sequence by 2009. Seven months later, Project

"Jim" – the complete genome sequence of James Watson, being the first sequence of an individual – was completed. Other applications of next generation sequencing are the targeting of DNA regions, metagenomics, transcriptome analysis and the identification of the genetic basis of disease and drug response.

All peer-reviewed publications enabled by 454 Sequencing technology (now pushing the 500 mark), can be browsed at www.454.com/publications-and-resources/publications.asp. -WK-