Danmark

Grateful disappointed

Pharmexa's leadership must be dumbfounded. In a fundraising exercise completed early in February, the Danish biotech company raised the very modest sum of €12 million. This is no more than a drop in the ocean when compared to the minimum of €46 million that Pharmexa declared they would need to maintain their present business strategy. However, there was apparently not much on offer to attract a weak European stock market. Pharmexa's disappointing mid-stage trial data for its liver cancer vaccine GV1001 didn't help, either.

Jakob Schmidt, Pharmexa's Chief Executive, seemed rather illogical in response, saying in an interview with Bioworld Today that he was, "grateful for the money [Pharmexa] got. [...] It's something to build on" but adding that he had,"... expected more." Schmidt's company has been the subject of rising speculation in recent months over the meltdown of their cash resources to less than €10 million. Pharmexa's share price has dropped nearly 80 percent within the last eight months.

Now, after a board meeting at Pharmexa's headquarters in Hørsholm, it has become clear what Schmidt meant when he predicted a few weeks ago that Pharmexa was considering "strategic alternatives and options". The Danish will focus solely on GV1001 and its universal influenza vaccine project whilst putting on hold their bone disease and early stage cancer projects as well as other smaller projects. In addition, Schmidt will reduce Pharmexa's headcount by 20 employees (leaving approximately 80) and move the business to a smaller facility in the research park in Hørsholm by May this year.

Given the fact that Pharmexa's cancer immunotherapy is an as yet unproven approach and that they lack dozens of millions of euros to proceed successfully, the Danish are facing an uncertain future.

Germany

Dwarfing the Giant

Since the failure of its prototype cancer drug, satraplatin, at the end of last year, the German company GPC Biotech (Martinsried) has lost nearly 90 percent of its share price and, in addition, most of its workforce.

In February, the weakened company's management declared a new round of layoffs that will cost the jobs of another 38 employees. After that, GPC will have only 14 workers in Munich and 49 in Princeton (USA). In better times, more than 300 people were employed by the former biotech starlet.

WINFRIED KOEPPELLE

RNAi therapy

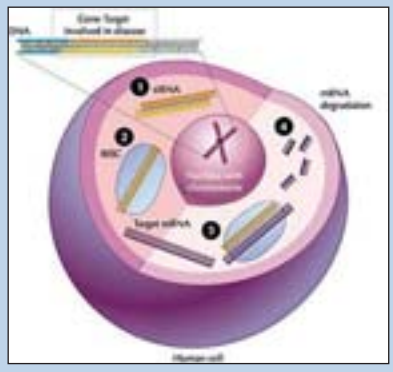
Evidence Found for the Magic Bullet?

Alnylam hasn't beaten cancer and AIDS but they have proved that RNAi therapy could work in humans.

After years of enthusiastic praise without concrete evidence, RNA interference (RNAi) has showed the first signs that it could have therapeutic uses in humans. Alnylam Pharmaceuticals, a biopharmaceutical company developing novel therapeutics based on RNAi, reported statistically significant anti-viral efficacy from a pilot Phase II study on its experimental drug for the respiratory syncytial virus, ALN-RSV01. Healthy patients who received ALN-RSV01 experienced an infection rate reduced by 38 percent compared to those patients given a placebo, Alnylam claimed in a press release.

Human respiratory syncytial virus (RSV) isn't a very dangerous pathogen. It is the major cause of lower respiratory tract infection during childhood, generating only mild symptoms, very similar to those of common colds. But in people with compromised immunity, however, RSV behaves more aggressively and can cause death.

Alnylam's ALN-RSV01 specifically initiates the destruction of the mRNA used to produce the RSV nucleocapsid protein, which is essential for viral replication. In the Phase II trial, the drug was delivered directly to infected lung cells, silencing the protein concerned, thus neutralizing the virus, and preventing viral spread and further infection.



RNA interference: probably working.

The company, headquartered in Cambridge, Massachusetts, was founded in 2002 by several pioneers of RNAi research, including RNAi co-discoverer Phillip D. Zamore, 1993 Nobel Prize winner Phillip Sharp and Thomas Tuschl from Germany, who discovered the structure of mammalian RNAi in 2001.

"Alnylam has demonstrated the first ever human proof of concept with an RNAi therapeutic," said John Maraganore, Chief Executive Officer of Alnylam, but he added that much more work needs to be done before the drug is proven to be truly effective. In fact, the trial had several weak points. Firstly, the number of participants was very low (only 88, of whom 43 got ALN-RSV01, the others a placebo). Secondly, RSV only becomes serious when it affects the lungs. In the trial, though, patients were infected and treated in their nose. Thirdly, the doctors involved didn't notice any difference between the clinical symptoms of patients treated with the experimental drug and those treated with a placebo.

However, that's no reason to cry foul. Alnylam's pilot Phase II trial was intended mainly to investigate one of RNAi's biggest hurdles: effective drug delivery to infected cells or tissues. Now Alnylam is about to start another Phase II clinical trial that will cover the pilot trial's weaknesses. -WK-

Genmab wrangles an antibody plant

Danish Dynamite goes America

Despite a huge net loss, the Copenhagen-based antibody developer has a strong cash position. Or should we say "had", given their recent purchase of a manufacturing plant in Minnesota, USA?

Danes dancing in the USA

Genmab (Copenhagen), a Danish developer of therapeutic antibodies, has signed a deal to buy an antibody manufacturing plant in Brooklyn Park, Minnesota (US). Its former owner, PDL Biopharma (once known as Protein Design Labs), will pocket €162 million in cash for it. According to Genmab officials, the transaction "also includes land, equipment and access to a leased space housing a development lab".

PDL has suffered clinical trial failures in recent years and regressed from biotech superstar to potential takeover target, losing more than 60 percent of its stock value since 2006. Despite trying to liquidate as many assets as possible, the firm is expected to be snapped up in the coming months.

In the light of these challenges, Genmab has (or had) an enviable problem. For a long time the Danish antibody maker has sought a sustainable source of both clinical and commercial scale antibody material, with no success. The Minnesota facility, with its four bioreactors and a production capacity of 22,000 litres, should be sufficient to solve this problem satisfactorily and enable Genmab "to transition three antibodies from research to manufacturing per year". According to Chief Executive Officer Lisa Drakeman, Genmab plans to retain the 170 employees currently working at the US manufacturing facility.

A big fish in Europe

Currently the Danish have ten antibody products in clinical development, intended for the treatment of diseases such as cancer and autoimmune disorders. The company employs approximately 250 people and recorded revenues of €16 million in 2006 (the financial data of 2007 haven't been published yet). In the same period, the net loss was nearly €50 million.

They won't worry about that in Copenhagen: Genmab ended 2006 in a strong position with €206 million in cash. Seeing this, GlaxoSmithKline snatched up Genmab's blood cancer and rheumatoid arthritis drug HuMax-CD20 to boost its oncology drug pipeline, disbursing €240 million for a 10 percent stake in Genmab as well as a €69 million licensing fee for HuMax. The deal (not the first for the Danish in 2006) should make Genmab profitable in 2007/2008. HuMax-CD20 has been tested in Phase III clinical trials for chronic lymphocytic leukemia and non-Hodgkin's lymphoma and in Phase II trials for rheumatoid arthritis. The antibody is widely considered to be a potential cash cow because it might one day compete with MabThera/Rituxan (sold by Roche/Genentech).

The first Danish biotech blockbuster?

MabThera yielded an incredible €3 billion last year. HuMax, if it reaches the market, could follow suit. With prospects like these, one mustn't be surprised at recent rumours that Biogen Idec, another leviathan, wants Genmab's new leukemia therapy (what would GSK say to that?). It seems that those 250 people in Copenhagen are poised for a relaxed future. W. Koeppelle

United Kingdom / Scotland

Light Plaster Combats Cancer

A Scottish start-up receives funding for a futuristic device.

Ever heard of PDT? You should have, because it's something that can be worth €3.3 million. This sum recently was given as equity funding to Lumicure Ltd. of St Andrews, Fife (located on the east coast of Scotland). Lumicure develops ambulatory light sources for skin treatment. The company's main project is a light-emitting "sticking plaster" for the treatment of skin cancer, used in Photodynamic Therapy (PDT) and cosmetic skin treatment.

Photodynamic therapy is a medical technology involving the application of a photosensitive drug followed by exposure to a selective light source which activates the drug and destroys the diseased cells, avoiding surgical removal of the tumour and the need for a hospital stay. PDT is an approved treatment for cancer and wet macular degeneration and is also being investigated for the treatment of psoriasis and acne. Lumicure develops low cost, portable and disposable light sources – thin films of organic material sandwiched between two electrical contacts, known as an organic light emitting diode (OLED), which can be used in PDT and cosmetic treatments. The original work on the "OLED sticking plaster" was carried out by two professors from St Andrews and Dundee. According to Lumicure, these devices are worn by the patient in a similar way to a sticking plaster, while the battery is carried like an iPod. -WK-

Nobel laureate decries HIV vaccine strategies

Getting Nowhere?

After 20 years of feverish research and billions of dollars spent, the US virus expert David Baltimore is critical of current strategies to combat the HI virus. "Perhaps", he says, "we will never find an AIDS vaccine."

When Microsoft founder Bill Gates donated another €195 million to worldwide HIV vaccine research in the summer of 2006, most commentators were still confident of an early victory over the pandemic immunodeficiency virus. With the more than half a billion dollars that the Bill and Melinda Gates Foundation has awarded towards the cause, the €2.3 billion that the NIH (National Institutes of Health) have contributed over the past 20 years and countless additional research grants, you would expect the brutal little virus to capitulate in a flash.

Far from it. The development of a protective HIV vaccine seems as distant as ever before. To date, nearly a hundred clinical phase trials of candidate vaccines have been conducted worldwide, but every single one has been ineffective.

While competitive scientists get increasingly frustrated, a Nobel Prize winning colleague is rubbing salt into their wounds. David Baltimore, a tumour virus researcher and former president of Caltech and Rockefeller University, recently declared publicly that scientists are no closer to developing a vaccine against HIV than they were two decades ago, when the first vaccine trials started in the USA. At the annual meeting of the American Association for the Advancement of Science (AAAS), Baltimore stated that there was little hope, after his colleagues said that attempts to pressure the virus with antibodies or to boost the human immune system have completely failed.

Nobel Prize winner David Baltimore is sceptical about getting an efficient vaccine against HIV soon.

"Our community has to undertake new approaches, or we might find ourselves with a worldwide epidemic and no effective response", the scientist warned. He favours novel approaches, such as gene and stem cell therapies: "We have to do better than nature. But perhaps," Baltimore suspects, "an AIDS vaccine might never be found".

Gel fails when vaccine takes first hurdle

In keeping with Baltimore's prophecies of doom, bad news emerged in February about a microbicide gel that was hoped to protect women against HIV. The gel (known as Carraguard), developed by the non-profit organisation Population Council, contains a sulfated polysaccharide that was suspected to bind viruses, thereby preventing them from annexing healthy cells. However, the crucial Carraguard Phase III trial was a complete failure. After 20 years of development, stunned researchers reported that women given the gel suffered 134 HIV infections, compared to 151 infections in the control group. That's a result close to nothing.

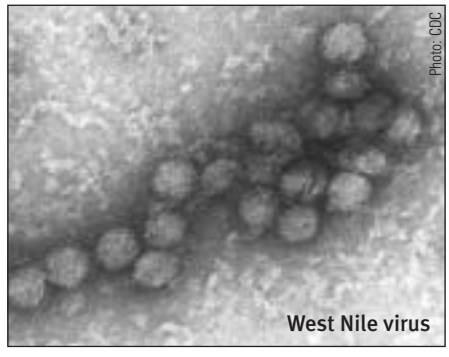
Winfried Koeppelle

The Netherlands

Insufficient Infections

Vaccine developer Crucell snubs patients and shareholders by postponing its West Nile virus programme.

Crucell, of Leiden (The Netherlands), the sixth largest vaccine company worldwide, has astonished patients, analysts and shareholders with the decision to postpone its development programme for a vaccine to prevent West Nile virus (WNV) in humans. The West Nile vaccine programme has always been considered one of the key therapies in Crucell's pipeline so far. Moreover, it demonstrated safety and tolerability in a recent Phase I trial. The reason for the unpopular decision was odd: fewer and fewer people are infected by the virus in the US. When Crucell launched the WNV programme, some 10,000 Americans were infected, promising lucrative earnings from a future vaccine. That figure dropped to 3,000 patients last year. Crucell didn't mention who will take care of them in future.



West Nile virus

However, we shouldn't be too harsh. With a huge net loss of €45.9 million in 2007, a commercial company like Crucell hasn't the financial means to continue with a project that will never make a profit. -wk-


Photo: wk

Original or copy? Generic drugs are on the advance.

Generics threaten pharmaceutical top dogs

Cloned Drugs on the Rise

Research-based pharmaceutical companies expect to lose billions of revenue in 2008. Now they are planning to fight back.

Heavy seas are ahead for the pharmaceutical industry this year. It expects to lose more than €15 billion in revenue when several blockbuster drugs go off patent in 2008. Some fast sellers, including Merck's osteoporosis drug Fosamax (with annual sales of at least €2.1 billion) and Johnson & Johnson's schizophrenia drug Risperdal (€2.8 billion) are expected to lose exclusivity in at least one market worldwide. Competitors like GlaxoSmithKline, Abbott Laboratories, AstraZeneca and Pfizer also face decreasing sales due to expiring patents.

One man's meat is another man's poison. Investors might be better off abandoning this sluggish industry and looking for greener pastures. An exceptionally sapid market, for example, is generics. Many analysts are bullish in their attitude to strong generics makers such as Teva and Actavis (Israel), Sandoz (Switzerland), Merck KGaA, Ratiopharm and Stada (all Germany). Outside Europe, one should watch India in particular. The country's biggest and world's 7th largest generics maker, Ranbaxy, is expected to increase its earnings by 41 percent this year.

Lobbyists take position

In the meantime, generics lobbyists have already positioned themselves carefully. In February, the US Generic Pharmaceutical Association (GphA) announced plans to launch a legislative programme intended to boost the share of generics in the US drug market (which has increased from 40 to almost 60 percent over the last seven years). In times of collapsing health care systems, the GphA is preaching to the converted.

Big Pharma is in a sorry state but unbeaten. Their new strategy runs as follows: If your blockbuster drug goes off patent, then sell your own generic at an unbeatably low price. Indeed, Pfizer intends to introduce a copy of its proprietary antidepressant Zoloft, which in 2006 was the most prescribed antidepressant on the US market with over 28 million prescriptions. According to reports in the US press, Pfizer's "second-rate Zoloft" will be sold significantly more cheaply than competitors' generics. Sounds like a drug price war to you, too?

Given the multi billions of euros that pharmaceutical companies earn every year this news won't grieve patients too much. Drugs getting cheaper? Well, health care politicians and insurers can start celebrating, too.

Winfried Koeppelle

"Wow, yeah, you need money, now give me money..."*

Biotech Funding in Springtime

Who received...	...what [€]...	...for which idea...	... when...	...from whom?
Fovea Pharmaceuticals (Paris/FRA)	30.0m	Treatments for ophthalmic diseases.	12/2007	Forbion Capital, Sofinnova, Abingworth, *et al.*
Santaris Pharma (Hørsholm/DEN)	20.4m	RNA antagonist drug candidates for Leukaemia.	12/2007	Gilde Healthcare Partners et al.
Ascendis Pharma (Copenhagen/DEN)	17.6m	Drugs for diabetes, CNS, and cardiovascular disease.	12/2007	Sofinnova, Gilde Healthcare, TechnoStart *et al.*
TcLand Expression (Nantes/FRA)	8.2 m	Immunoprofiling and gene expression biomarkers.	12/2007	Auriga Partners *et al.*
Circassia (London, UK)	8.0m	Immunotherapy (development of an allergy vaccine).	02/2008	Imperial Innov., Landsdowne, Tudor Capital.
Photopharmica (Leeds/UK)	7.9m	Pharmaceutical products using photodynamic therapy.	01/2008	IP Group.
Prosonix (Oxford/UK)	6.6m	Ultrasonic process chemistry solutions.	12/2007	Solon Ventures, Entrepreneurs Fund, *et al.*
Caprotec Bioanalytics (Berlin/GER)	6.0m	Mass spectrometry for analyzing protein mixtures.	01/2008	Creathor Venture, IBB, ERP Startfonds, *et al.*
New Earth Solutions (Canford/UK)	5.3m	Biological waste treatment.	02/2008	Impax Asset Management.
Tissue Regenix (Leeds/UK)	4.0m	Tissue products that regenerate inside the body.	02/2008	n/a
Pantec Biosolutions (Ruggell/LI)	3.8m	Laser micro-poration technology for delivery of drugs.	12/2007	Gamma Capital Partners *et al.*
Lumicure (St Andrews, Fife/UK)	3.3m	Ambulatory light sources for skin treatment.	02/2008	Longbow Capital LLP, Scottish Venture Fund.
Verona Pharma (London/UK)	3.1m	Respiratory drugs against asthma and hayfever.	01/2008	Placing of new shares on AIM.
Atlas Genetics(Bath, UK)	2.7m	Molecular diagnostics.	02/2008	South West Ventures, Finance South West, *et al.*
Optimata (Ramat Gan, Israel)	1.0m	Discovery of cancer drugs.	02/2008	Group of private European investors.
Medigene (Martinsried, Germany)	0.6m	Immunology research.	02/2008	Fed. Ministry of Education and Research.
Abcellute (Cardiff/UK)	0.5m	Preserving cells without freezing them.	12/2007	n/a
Glycomar (Oban/UK)	0.3m	Potential marine anti-inflammatory drugs.	12/2007	Highlands & Islands Enterprise.

**The Beatles (1963): Money (That's What I Want), composed 1959 by Janie Bradford and Berry Gordy.*