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NuCana BioMed Gets $10.5M For ProTide Cancer Drugs

By Cormac Sheridan
***BioWorld International* Correspondent**

NuCana BioMed Ltd. raised £6.74 million (US$10.5 million) in a Series A round to advance a series of modified nucleoside analogues in cancer indications and has set its sights on becoming the Inhibitex Inc. or even the Pharmasset Inc. of the cancer world.

The company's co-founders, CEO Hugh Griffith and executive chairman Chris Wood, previously led New York-based cancer drug developer Bioenvision Inc., which they sold to Cambridge, Mass.-based Genzyme Inc. for $345 million.

They started NuCana BioMed in 2008 and obtained the rights to a prodrug technology, called ProTide, for application in cancer indications. It incorporates one of

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Galapagos Seeks Partner on Heels of Strong RA Drug Data

By Nuala Moran
***BioWorld International* Correspondent**

LONDON – Galapagos NV reported strong efficacy data from a Phase IIa proof-of-concept study of its selective Janus kinase 1 (JAK 1) inhibitor GLP0634 in rheumatoid arthritis and said it is now in partnering discussions.

The field of JAK inhibitors was enlivened earlier in November by the FDA's approval of the first drug in the class to reach the market, Incyte Inc.'s Jakafi, (ruxolitinib) a treatment for the rare blood cancer myelofibrosis. And with Pfizer Inc.'s U.S. filing for the first JAK inhibitor for rheumatoid arthritis imminent, the Galapagos data prompted a 22 percent increase in the share price to €7.14 (US$9.53).

Although only an exploratory study with 36 patients,

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New Analgesic Compounds May Target Paracetamol Receptor

By Sharon Kingman
***BioWorld International* Correspondent**

LONDON – The mechanism of action of paracetamol has been unveiled, leaving the way clear for the development of new analgesics that are more effective and safer than paracetamol itself.

Researchers from Lund University, Sweden and King's College London, UK, have found that the breakdown product of paracetamol that causes liver toxicity is the same compound that is responsible for the analgesic activity of the drug.

"The mechanism of action of paracetamol has been a great mystery up until now. Our findings show that it may not be possible to use paracetamol as the lead compound to develop this drug into a more effective analgesic," Edward Högestätt, professor of clinical pharmacology at Lund University, told *BioWorld International*.

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Immunicum Closes Funds for Dendritic Cell Vaccine Trial

By Cormac Sheridan
***BioWorld International* Correspondent**

Immunicum AB is finalizing the first closing of an SEK25 million (US$3.6 million) financing round to take forward a series of therapeutic vaccine technologies for treating cancer.

The Gothenburg, Sweden-based company, a spinout from Sahlgrenska University Hospital in Gothenburg, is planning to begin its first clinical trial next year, involving a therapeutic vaccine based on the administration of allogeneic dendritic cells, in patients with renal cell carcinoma.

"Usually when you talk about dendritic cell vaccines, people assume you mean it's autologous dendritic cells," CEO Jamal El-Mosleh told *BioWorld International*. "What our researchers have found is you can use allogeneic dendritic cells to create an inflammation that is desirable."

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NuCana

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the key medicinal chemistry innovations underlying the spectacular rise of nucleoside analogue drugs in hepatitis C virus (HCV) therapy, which has led to the recent $11 billion bid by Foster City, Calif.-based Gilead Sciences Inc. for Pharmasset, of Princeton, N.J., and to buyout speculation centering on Alpharetta, Ga.-based Inhibitex.

Chris McGuigan, professor of medicinal chemistry at Cardiff University, in Wales, developed the ProTide technology, and he is a board member of Inhibitex, which has applied his approach to its HCV drug INX-189.

NuCana is applying the same technology to cytotoxic cancer drugs in the hope that it will substantially improve both efficacy and tolerability.

It involves the production of nucleoside phosphoramidites as prodrugs of active nucleoside triphosphates or diphosphates. That is accomplished by the addition of a monophosphate group to a nucleoside molecule.

Although that reaction normally happens within the cell, it is an inefficient and rate-limiting step that greatly hampers the efficacy of traditional nucleoside analogues.

The nucleoside phosphoramidite species is further modified by the addition of aryl, ester and amino acid groups to protect the charged entity during its passage through the cell membrane.

"There are over a million different combinations for each nucleoside," Griffith told *BioWorld International*. "Only some would confer the advantages we're looking for." Understanding which molecules do is a key component of the company's expertise.

NuCana's lead compound is a modified version of gemcitabine, a new chemical entity called NUC-1031, which is entering clinical development early next year. Several others are lined up to follow. "This [funding round] will enable us to take three of our compounds into the clinic and to get Phase II data on two of them," Griffith said. After gemcitabine, NuCana will work on a modified version of 5-fluorouracil, which should enter the clinic in late 2012.

By virtue of its modifications, NUC-1031 is a lipophilic molecule and is transported passively through the cell membrane rather than relying on the human equilibrative nucleoside transporter-1 (hENT1), which gemcitabine requires. That bypasses one of the resistance mechanisms that can occur in cancer patients who receive the drug; that is low expression of hENT1.

But NUC-1031 also bypasses two other resistance mechanisms associated with gemcitabine therapy. It is not affected by low levels of deoxycytidine kinase, the enzyme that normally catalyzes the first phosphorylation step, as that has already been accomplished during drug synthesis. It also is not susceptible to cytidine deaminase cleavage, which can break down the monophosphorylated species before the additional phosphorylation steps necessary for the production of the active drug can occur. High levels of that enzyme can also cause resistance.

Moreover, the deamination step can give rise to toxic uridine metabolites, which can create tolerability problems. In preclinical toxicology experiments, NUC-1031 was tolerated at doses up to four times the dose at which gemcitabine was tolerated, Griffith said.

"The ProTides generally appear to be far better tolerated than the parent nucleoside analogues," he added.

NuCana's approach is similar to, but goes beyond, that being pursued by Clavis Pharma ASA, of Oslo, Norway, and its partner, Boulder, Colo.-based Clovis Oncology Inc., which are developing CP-4126 (CO-101) a version of gemcitabine that has been modified by the addition of an elaidic acid lipid tail. That also enables the molecule to enter cells by passive diffusion. "It still doesn't overcome the other key resistance mechanisms," Griffith said. CP-4126 is undergoing a pivotal Phase IIb trial as a first-line therapy in patients with metastatic pancreatic cancer.

The current round was oversubscribed and was led by Sofinnova Partners, while Morningside Ventures, Scottish Investment Bank's Scottish Venture Fund and Alida Capital International Ltd. also participated.

The company previously raised £3 million in seed funding from Edinburgh-based Alida, a business angel network of which Griffith and Wood are members, and Scottish Enterprise. ■

Other News To Note

• **AstraZeneca plc**, of London, and **Bristol-Myers Squibb Co.**, of New York, gained a European label expansion for diabetes drug Onglyza (saxagliptin). The DPP-4 inhibitor is now approved for use with insulin.

• **BioLineRx Ltd.**, of Jerusalem, said it received approval from Indian regulators to start the Phase II/III CLARITY trial of BL-1020, an oral GABA-enhanced antipsychotic for treating schizophrenia. Overall, the study is expected to be conducted at about 18 sites in India, 14 sites in Romania and four sites in Israel. About 450 patients will be enrolled, and the goal is to determine the short-term and long-term cognitive efficacy, as well as the antipsychotic efficacy, safety and tolerability of the drug over periods of six weeks, 12 weeks and 24 weeks.

• **Bionor Pharma ASA**, of Oslo, Norway, presented data relating to its universal influenza candidate, Vacc-Flu, at the Influenza Congress USA in Arlington, Va. The vaccine targets conserved regions of the viral genome that are common to all influenzas. Mice vaccinated with Vacc-Flu had 25 percent more protection from influenza when challenged with a different strain compared to a conventional flu vaccine.