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FINANCINGS

By Cormac Sheridan, Staff Writer

High tide for protides: Nucana Biomed pulls in $57M series B

Buoyed by unexpectedly early signs of robust clinical efficacy for its lead protide cancer drug Acelarin (NUC-1031), Nucana Biomed Ltd. raised $57 million in a series B round to accelerate its development and to advance several others into the clinic.

Acelarin, a modified version of the widely used nucleoside analogue gemcitabine, has elicited strong responses in an ongoing phase I trial in patients with advanced cancer.

"The data we've got in the phase I has ticked that efficacy signal box," Nucana co-founder and CEO Hugh Griffith told BioWorld Today. "We haven't yet reached the recommended phase II dose."

Despite Acelarin's early stage of development, the company and its investors are attaching high expectations to the drug.

A benchmarking exercise comparing it with other anticancer agents at the same stage of development has further heightened the optimism.

"Acelarin is as good as if not better than all the anticancer agents we were able to look at," Griffith said.

The open-label trial has recruited 44 patients so far. "All patients had rapidly progressing disease on entry, and over 90 percent had metastatic disease," Griffith said. Some, even those who were end-stage cancer patients, have had disease control for more than a year at this point, despite having an expected survival of about 12 weeks. The company will report efficacy data at the American Society of Clinical Oncology meeting in Chicago in the coming weeks. It will also recruit about 35 more patients, to enrich the study population with cancers that are of immediate interest.

The Edinburgh, UK-based company plans to move Acelarin into two or three phase II/III trials later this year, which, with the blessing of drug regulators, could be pivotal studies. It has yet to finalize its lead indications, but the frontrunners include pancreatic cancer, cholangiocarcinoma (bile duct cancer), ovarian cancer and non-small-cell lung cancer.

"We have several options, because we've seen activity across such a broad range of solid tumor types," Griffith said.

Nucana is applying to cancer the same medicinal chemistry approach that underpins sofosbuvir (Sovaldi), the drug marketed by Foster City, Calif.-based Gilead Sciences Inc., which is poised to revolutionize the treatment of hepatitis C virus (HCV) infection.

It involves the modification of existing nucleoside analogues by the addition of a phosphoramidite moiety to form prodrugs of active nucleoside triphosphates or diphosphates. This eliminates the requirement for active transport across the cell membrane and for kinase-mediated phosphorylation within the cell, both of which can be inefficient or dramatically altered in treatment-refractory cancers.

One of the reasons underlying the poor response rate of gemcitabine – Nucana puts it at 5 percent – is the absence or the low expression of deoxycytidine kinase, which is needed for phosphorylation of the nucleoside. "That's probably the key enzyme," Griffith noted. The protide version of the drug is also resistant to cleavage by cytidine deaminase, which inactivates gemcitabine and which is present at high levels in about half of patients.

Acelarin also contains aryl, ester and amino acid groups to protect the charged molecule during its passage, by passive diffusion, across the cell membrane. Unlike gemcitabine, it does not require the human equilibrative nucleoside transporter-1 (hENT1) protein, low levels of which constitute another cancer resistance mechanism.

Clavis Pharma ASA, of Oslo, Norway, and Boulder, Colo.- based Clovis Oncology Inc., co-developed CO-101, a version of gemcitabine modified with an elaidic acid lipid tail to override this issue, but the drug failed a phase II trial in pancreatic cancer.

"Unfortunately it appeared that that agent was deaminated very quickly," Griffith added. "It also needed deoxycytidine kinase."

Sofinnova Ventures led the new funding round, while existing investors Sofinnova Partners, Morningside Ventures, Alida Capital International and the Scottish Investment Bank also participated.

"This wasn't a roadshow where we went out to talk to 50 VCs. It was a very targeted transaction," Griffith said.

The company's founders, Griffith and Nucana's executive chairman, Chris Wood, previously led New York-based Bioenvision Inc., which Genzyme (now part of Paris-based Sanofi SA) acquired for $345 million in 2007.

Sofinnova Ventures has been following Nucana for some time, general partner James Healy told BioWorld Today. "It's a combination of a proven management team – they did a great job with Bioenvision – and the Protide technology, which has the potential to change how patients with refractory cancer are treated," he said. "It's a very large patient population they're addressing, with a very large unmet medical need."

Behind Acelarin, Nucana is lining up NUC-3373 – a protide version of 5-fluorouracil and floxuridine – for clinical trials later this year, and it plans to move two more drugs into the clinic in 2015.

"We see a lot of value creation over the next two years," Healy said.

Rafaèle Tordjman, managing partner at Paris-based Sofinnova Partners, attributed the company's progress to the "outstanding execution" of Griffith and his team. "We would like to clone them," she told BioWorld Today. The company raised £6.74 million (US$11.3) million in a series A round in late 2011 and another £3 million in seed funding. (See BioWorld Today, Nov. 30, 2011.) //