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Clavis joins no-hope league as Elacyt strikes out

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The final word on Clavis Pharma was written in the numbers. Its phase III Clavela study of Elacyt was an unambiguous failure, failing to extend the lives of acute myeloid leukaemia patients when compared to alternative treatments, with subgroup analyses turning up no hope of a pathway to approval.

With failure casting doubt over its remaining portfolio of products, the Norwegian group is now looking like it will wind itself up or become a merger target for its cash and market listing. Its fate shows the danger of investing in a single technology. At least, unlike many other biotechs, the Clavis executive team signalled that it would give up in the event of Elacyt's failure (*Event – Do or die for Clavis in leukaemia trial, February 26, 2013*).

Red flag

Clavis shares fell 81% to NKr1.26 in mid-afternoon trading, valuing the company at NKr42.5m ($7.3m). Given that shares were at cash levels even before this latest drop, the company could make an attractive target for a private biotech searching for a market listing; it reported the equivalent of $38.3m in cash at the end of 2012.

The writing on the wall for Clavis may have been the earlier failure of CP-4126, which like Elacyt was an older chemotherapy that was hoped to be a more effective compound through the use of Clavis' lipid vector technology (*Leap failure sends Clavis and Clovis crashing back to earth, November 12, 2012*). CP-4126 is a modified version of gemcitabine intended for pancreatic cancer. Elacyt is cytarabine.

In both cases, the hypothesis was that low levels of the transporter protein hENT1 prevent the active ingredient from entering the cells; the lipid "tail" attached to the chemotherapeutic compound extends its half-life, allows it to enter cells independently of hENT1 and remain active in the cells longer. The failure of '4126 in the phase III Leap trial was clearly a big red flag for Clavela.

Clear-cut

Clavis said median survival in the Elacyt arm was 3.5 months, compared with 3.3 months in the control arm. To achieve statistical significance, Elacyt needed to achieve 4.5 months of survival against three months in the control arm.

In the control arm, trial physicians were allowed to choose treatments; the most common one was fludarabine, cytarabine and granulocyte colony-stimulating factor, with or without idarubicin.

Company executives said investigators could identify no significant differences in subgroups. With all work suspended on the compound, senior management have signalled they have no intention of conducting any retrospective data mining to keep hope alive.

With its only clinical-phase product shelved, the company will now seek to cut costs and review its strategic options. Dissolving the company and giving remaining cash to shareholders is one option; chief executive Olav Hellebø said Clavis has a short list of potential buyers and will begin discussions with those suitors shortly.

With such a unanimous verdict on the clinical promise of its technology, the executive team should be praised for taking a clear-cut decision to wind up the project. The risk of failure is inherent in drug development; Clavis could be a case study in how to handle failure when it comes.

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