Clovis goes pre-clinical to sign NSCLC programme

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Clovis Oncology has gone down the R&D pipeline to sign its second deal, sewing up Avila Therapeutics’ pre-clinical programme targeting epidermal growth factor receptor (EGFR) in non-small-cell lung cancer (NSCLC) in a deal valued up to $209m.

Following through on an aim to sign at least two candidates in 2010, Colorado-based Clovis will develop and commercialise Avila’s covalent platform that seeks to combat clinical resistance to Tarceva and Iressa in NSCLC (EP Vantage Interview – Clovis up and running and seeking more deals, December 3, 2009). Avila’s platform aims to effectively silence disease-causing proteins with permanent bonds to very specific targets, with the hope of better efficacy, tolerability and safety (EP Vantage Interview - Avila's covalent drugs looking highly attractive, September 25, 2009).

Targeting a mutation

EGFR is a cell surface receptor, and among other functions is involved in cell proliferation. Mutations that lead to over expression of EGFR can lead to cancer, in particular lung, colon and brain cancer.

In lung cancer the small molecule tyrosine kinase inhibitors Tarceva and Iressa work by blocking the EGFR receptor, preventing it from activating and effectively halting a signalling cascade that helps a tumour grow and spread.

However, Tarceva and Iressa are non-selective and block all EGFRs, mutant or not, hence their side effects elsewhere in the body. Additionally, in about half of all lung cancer cases clinical resistance arises as the tumour cells develop a mutation called T790M, rendering the drugs ineffective.

Avila’s programme targets both T790M mutations and the initial activating EGFR mutations that cause the lung cancer in the first place, whilst sparing the normal EGFRs elsewhere in the body. The companies hope this will lead to a candidate effective in both first-line and refractory settings with a much improved side effect profile.

Under the deal, Avila received an upfront fee and will be eligible for development, regulatory, and sales-based milestones, tiered royalties and selected sublicense income. Specific values were not disclosed.

The privately-held companies will collaborate on pre-clinical development, dubbed the EGFR mutant selective inhibitor (EMSI) programme. Clovis will be responsible for development and commercialisation, including developing a companion diagnostic to identify the key mutation.

Looking for candidates

Aided by a $145m first funding round a year ago, Clovis already has a cancer drug in its pipeline, the pyrimidine analogue CP-4126, which was in phase II when it licensed the drug from Clavis Pharma. But with competition growing for early-stage assets Clovis, like much of the industry, went further upstream in making its second deal, even though chief executive Patrick Mahaffy told EP Vantage he was looking for phase I-ready or phase I/II candidates (Product deals continue decline in 2009 but early stage assets gain value, February 23, 2010).

But like CP-4126, Avila’s programme is targeting a subset of patients who are not responding to treatment for identifiable reasons – in the case of CP-4126, the biomarker for hENT1, a transporter protein.

Mr Mahaffy has said he envisioned that bringing on five compounds at the development stage in four or five years would take Clovis to its operational and financial limits. As the Avila pre-clinical programme could yield multiple development-stage candidates it is not clear where the Avila deal puts the company in terms of its resource limits.
But it is clear that Clovis is following through on its purpose of targeting candidates addressing a specific and clearly identifiable unmet medical need.