Avacta

AVA6000 set to start US Phase I studies in early-2022

29 November 2021

- Avacta has received FDA approval to start Phase I studies of AVA6000 in the US. The IND clearance, ahead of our expected timeline, allows the current UK study (ALS-6000-101) to be expanded into US clinical sites. This first-in-human study, which started at the end of August, is an open-label, multi-centre trial investigating intravenous (IV) AVA6000 monotherapy in up to 80 patients with locally advanced (unresectable) and/or metastatic FAP-positive solid tumours. It consists of an initial dose escalation phase followed, if successful, by a dose expansion phase.
- AVA6000 is a FAP-activated prodrug of the established cytotoxin doxorubicin and is the first of Avacta's therapeutic programmes based on its proprietary pre|CISION technology. This exquisitely exploits the fact that FAPα (fibroblast activation protein alpha) protease enzyme is highly upregulated in over 90% of solid tumours, yet its expression is very low in most healthy adult tissues. pre|CISION employs a substrate that is sensitive to cleavage by FAPα, creating a novel drug that is only activated in the tumour site. This selectively increases active drug concentration at the target site and reduces overall systemic levels.
- Doxorubicin is an effective and widely used anthracycline chemo-therapeutic that is part of standard of care in several tumour types. Cumulative toxicity, especially cardiotoxicity, typically limits its use to only six cycles (typically 60-75mg/m^2 every three weeks until 450mg/m^2 is reached). Despite its toxicity limitations, and being a generic drug, doxorubicin consistently posts global sales of over $1bn annually. AVA6000 offers the prospect of enabling more treatment cycles to be carried out before reaching the cumulative cardiotoxic dose. If proven successful, the US and EU market opportunity is estimated at c $1.5bn pa in advanced soft tissue sarcomas, breast, and ovarian cancers.
- Completion of the UK Phase Ia dose escalation is expected by Q222, and that of the Phase Ib dose expansion anticipated by mid-2023. Patient enrolment in the first US clinical site is expected to start in early-2022. The dose escalation stage, involving c 20 patients with a variety of locally advanced or metastatic solid tumours, will determine safety and tolerability (although some efficacy signals may be noted) and establish the recommended dose for the Phase Ib stage. This will confirm safety and tolerability and explore preliminary anti-tumour activity.

Price	120p
Market Cap	£304m
Primary exchange	AIM
Sector	Healthcare
Company Code	AVCT
Corporate client	Yes

Company description:

Avacta owns two novel technology platforms: Affimer and pre|CISION. Affimer proteins are antibody mimetics being developed as diagnostic reagents and oncology therapeutics. pre|CISION improves potency and reduces toxicity of cancer drugs by only activating them inside the tumour. Successful clinical trials would be transformative for Avacta.

Trinity Delta view: The extension of the AVA6000 Phase I study into the US, ahead of our expectations, is an endorsement of Avacta's clinical team's efforts and the quality of the preclinical package. Positive outcomes in reducing doxorubicin's systemic toxicity will be important in establishing proof of concept of the pre|CISION platform. A broader pipeline of pro-drugs whose clinical utility would benefit from improved efficacy and reduced toxicities is being progressed. We value Avacta at £710m, or 280p per share, with the Diagnostic opportunities representing £133m and the Therapeutic pipeline rNPV £559m.

Analysts

Lala Gregorek
lgregorek@trinitydelta.org
+44 (0) 20 3637 5043

Franc Gregori
fgregori@trinitydelta.org
+44 (0) 20 3637 5041

Lala Gregorek lgregorek@trinitydelta.org
+44 (0) 20 3637 5043

Franc Gregori fgregori@trinitydelta.org
+44 (0) 20 3637 5041

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