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Accession – Clinical

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Abstract:
A phase 1 study of ATTR-01, a novel oncolytic adenovirus targeting αvβ6 integrin, which expresses an anti-PD-L1 antibody in tumors following IV delivery in patients with selected epithelial cancers.

Oncolytic viruses encoding transgenes represent a tractable single-agent approach to targeted delivery of immunomodulatory therapies to tumors, and have emerged as a promising modality in cancer therapy. TROCEPT is a next-generation genetically modified adenovirus type-5, rationally designed to overcome the limitations of existing IV delivered viruses and to increase tumor exposure. TROCEPT is uniquely de-targeted to avoid uptake by healthy cells, including the liver, by removal of normal cell tropisms, and is re-targeted to specifically infect and replicate in tumor cells that express the cancer marker αvβ6 integrin. ATTR-01 is a first-in-class transgene modified variant of TROCEPT that, following infection of permissive tumor cells, expresses an anti-PD-L1 antibody. Expression of the anti-PD-L1 checkpoint inhibitor locally, rather than via systemic delivery by IV infusion, may lead to higher local (tumor) concentrations of the drug and avoid exhaustion of systemic T cells, thereby increasing efficacy and reducing off-tumor toxicity.

ATTEST utilises a complex innovative design to explore dose, regimen, safety, efficacy and long-term treatment outcomes of ATTR-01. Co-primary objectives are to characterise the safety and tolerability of ATTR-01 and identify a recommended dose. Preliminary efficacy, immunogenicity and viral persistence are secondary endpoints. Exploratory endpoints include pharmacodynamic outcomes in tumor tissue and blood. The first sub-protocol is a phase 1, open-label, dose escalation/expansion study. Part 1 is a dose escalation, using a Keyboard design, up to a maximum dose of 1×10^{13} viral particles ($n \leq 48$ participants). Up to two doses will be expanded in Part 2 to explore the optimal dose(s) ($n \leq 24$ participants). Participants will be recruited having progressed after ≥ 1 line of standard of care therapy with six cancer types (non-small cell lung, urothelial, head and neck, pancreatic, endometrial, cholangiocarcinoma) that typically demonstrate a high frequency (≥ 75%) and high level of αvβ6 integrin expression. Recruitment was initiated in Q4 2025.