ALT-801 (Tumor-targeted IL-2 immunotherapeutic)

**FACT SHEET**

ALT-801 is an investigational agent and has not been approved by regulatory agencies.

**Background:** ALT-801 is an innovative immunotherapeutic fusion protein consisting of interleukin-2 (IL-2), an approved cytokine for treatment of metastatic melanoma and renal cell carcinoma, linked to a single-chain T-cell receptor domain (STAR™). Through this fusion, ALT-801 changes the functional activity of the IL-2 domain. As shown in comparative pharmacokinetic, biodistribution, pharmacodynamic, tolerability and efficacy studies in experimental animal models, ALT-801 exhibits more potent immunostimulatory and antitumor activities against solid and hematological malignancies than IL-2. Thus, ALT-801 is expected to provide greater efficacy, lower toxicity, more convenient treatment regimens and a better quality of life for patients with cancer.

The STAR™ targeting domain of ALT-801 was developed through Altor’s STAR™ technology platform to recognize cancer cells that overexpress the tumor-associated antigen, p53. The p53 protein is mutated and overexpressed in roughly 50% of all human cancers and typically correlates with poor prognosis, making it an ideal target for a targeted therapeutic. However, p53 cannot be used as a target for antibody-based therapies because it is an intracellular protein not displayed on the cell surface. The soluble STAR™ domain of ALT-801 was generated from a high affinity TCR that binds to a peptide antigen derived from p53 and displayed in the context of HLA-A*0201 (Zhu, et al. 2006). When fused to IL-2, this STAR™ domain promotes targeting of immunostimulatory activity to the site of p53-overexpressing tumor cells, thereby localizing immune effector cytotoxic activities to the tumor microenvironment. This fusion protein also binds to and activates immune cells differently than IL-2 and has a longer in vivo half-life with extended localization in immune organs when compared to IL-2. Together, these properties provide ALT-801 with significantly greater antitumor activity than IL-2 against both p53-overexpressing and non-target-bearing tumors in various animal efficacy models (Card, et al.2004; Belmont, et al. 2006; Wen, et al. 2008).

**Clinical Development of ALT-801:** ALT-801 is the first TCR-based therapeutic to enter clinical trials and has been administered to over 100 patients with various cancer indications.

A $3 MM NCI-SBIR Bridge grant has been awarded to Altor to help fund the Phase 2 ALT-801 clinical trials and Altor was named as a “Success Story” by the Small Business Innovative Research program of NIH/NCI (NCI-SBIR Success Stories).
Phase | Investigational Therapy | Trial Number | Trial Description
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I | ALT-801 | NCT00496860 | Phase I Study of ALT-801 in Patients With Progressive Metastatic Malignancies*
I | ALT-801 + cisplatin | NCT01029873 | A Phase 1 Study of ALT-801 With Cisplatin in Patients With Metastatic Melanoma
II | ALT-801 + cisplatin + gemcitabine | NCT01326871 | A Study of ALT-801 in Combination With Cisplatin and Gemcitabine in Muscle Invasive or Metastatic Urothelial Cancer
I | ALT-801 + gemcitabine + BCG | NCT01625260 | A Study of ALT-801 in Patients With Bacterial Calmette-Guerin (BCG) Failure Non-Muscle Invasive Bladder Cancer


**Publications:**


More detailed documentation on ALT-801 may be provided under a confidentiality agreement.

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