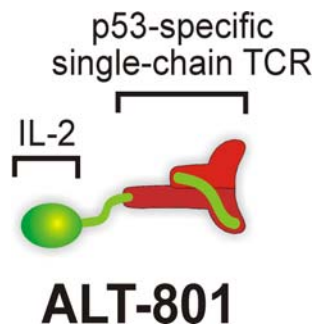


ALT-801 Fact Sheet



STAR™ Fusion Drugs for Cancer: Altor's lead product based on the STAR™ (Soluble T-cell Antigen Receptor) technology platform is **ALT-801**. This anti-cancer agent is a recombinant soluble T-cell receptor-cytokine fusion protein that targets cancer cells through the tumor-associated antigen, p53. The p53 tumor suppressor is mutated and over-expressed in roughly 50% of all human cancers and typically correlates with poor prognosis, making it an ideal target candidate 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. Using its STAR™ technology, Altor has developed a high-affinity single chain T-cell receptor (scTCR) that recognizes a peptide antigen derived from p53 and displayed in the context of HLA-A*0201. ALT-801 is a fusion of the p53-specific scTCR and IL-2, an approved anti-cancer cytokine, and is designed to deliver the IL-2 directly to the tumor

site providing greater efficacy, lower toxicity, more convenient treatment regimens and better quality of life for patients.

Preclinical efficacy studies using ALT-801 in solid tumor xenograft models have demonstrated that ALT-801 reduces experimental lung metastasis and inhibits the growth of well-established primary subcutaneous tumors in a dose-responsive manner. In all of these studies, ALT-801 had a significantly greater anti-tumor effect than free recombinant IL-2 or an irrelevant scTCR/IL-2 fusion protein on an equal molar basis. Altor's scientists have elucidated the mechanism-of-action of ALT-801, which appears to bind to and guide IL-2-responsive immune effector cells to the tumor site where they mediate their potent antitumor cytotoxic activities. This mechanism of action of the STAR™-cytokine fusion protein differentiates it from that of therapeutic antibodies and may explain the fusion protein's highly potent activities against tumors in animal efficacy models. These studies were supported in part by various Small Business Innovation Research (SBIR) grants from National Institutes of Health (NIH)/National Cancer Institute (NCI).

Altor intends to use ALT-801 as a replacement for recombinant human IL-2 (Proleukin®) that is currently approved for metastatic melanoma and renal cell carcinoma. In preclinical animal studies and in a recently completed Phase 1/2a study in patients with metastatic malignancies, ALT-801 showed a serum half-life of approximately 4 hours, a substantial increase over the 20-minute half-life observed for IL-2. The longer half-life of the fusion protein allows for a simpler dosage regimen than the every-8-hour infusion schedule currently used for high-dose IL-2 therapy. The improved stability and tumor-targeting nature of this fusion protein gives it the properties for it to be used at a lower dosage, which reduces its toxicity. Overall, ALT-801 shows promise as an improved targeted IL-2 cancer therapy.

Clinical Development: Altor's long-term clinical objective is to develop ALT-801 as a targeted immunotherapeutic with better antitumor potency, a lower toxicity profile and more convenient dosing schedule compared to that of human recombinant IL-2 and to expand its clinical utility beyond metastatic melanoma and renal cell carcinoma. Altor has completed an open-label, dose-escalating Phase 1/2a clinical trial (<http://clinicaltrials.gov/NCT00496860>) in which twenty-six patients with various metastatic, refractory malignancies were enrolled and infused with at least one dose of ALT-801. Results indicate that ALT-801 is well tolerated at the MTD and exhibits evidence of clinical benefit to cancer patients with 40% of the patients having stable disease, several with tumor shrinkage and one patient with a complete response (CR). The patient with the CR is still in complete remission more than 2 years post dose without other anti-cancer therapy. This suggests that ALT-801 can provide a durable response in patients with metastatic malignancies and mirrors that of high-dose IL-2 treatment but without the severe toxicities associated with high-dose IL-2 treatment. This trial was partially supported by an Orphan Products Development Grant from the US FDA. The results of this Phase 1/2a clinical trial can be summarized as follows:

- Completed open-label Phase 1/2a trial in p53 overexpressing/HLA-A*0201+ patients (n=26) with metastatic malignancies
- Favorable PK Profile: C_{max} as expected based on dosage, $t_{1/2}$ ~4 hrs
- Positive immune response: NK Cell Activation, Serum IFN γ ~4-8 hrs post dose, No TNF α
- Well-tolerated at MTD (0.04 mg/kg)
 - Significantly less grade III or IV adverse events than high-dose IL-2
 - Retreatment well-tolerated
- Encouraging evidence of clinical benefit in end-stage patients
 - CR in metastatic melanoma patient & 40% treated patients had stable disease / tumor shrinkage
 - Various indications (Melanoma, RCC, Prostate, Head & Neck) showed benefit
- Higher dose (0.08 mg/kg) shows superior clinical benefit in Malignant Melanoma

ALT-801 + Cisplatin Phase 2 Trial for Metastatic Melanoma: A Phase 1b/2 clinical trial using ALT-801 in patients with locally advanced or metastatic melanoma started enrolling patients in Q1-2010 (<http://clinicaltrials.gov/NCT01029873>). The trial was designed to use ALT-801 in combination with cisplatin. The treatment, which comprised with four dosing cycles, is administered in an outpatient setting. The adjuvant use of cisplatin for this trial is due to: (1) the reported tolerability of cisplatin in IL-2 based biochemotherapy regimens for melanoma, (2) the anti-melanoma effect of cisplatin, (3) the ability of cisplatin to increase the target density of ALT-801 by up-regulating tumor p53 expression and display, and (4) the demonstration of strong synergistic effect of cisplatin to ALT-801 in Altor's pre-clinical studies.

The primary objectives of the trial are to determine the MTD of the ALT-801+Cisplatin regimen during the dose escalation stage and to evaluate the safety of the ALT-801+Cisplatin regimen, assess the objective response (OR) of the tumors, which includes complete responses (CR) and partial responses (PR), and assess the clinical benefit (CB) of the ALT-801+Cisplatin regimen, which includes CR, PR and stable disease. The secondary endpoints include assessment of the patient's six-month and one-year survival rates. Survival of all enrolled patients at 6 and 12 months from the start of study treatment will be evaluated. In the initial Phase 1/2a, ALT-801 was administered daily in an in-patient setting in weeks 1 and 3, whereas in this Phase 1b/2 trial, ALT-801 is infused every other day in an out-patient setting. The ALT-801+Cisplatin regimen has been well-tolerated and patient treatment at escalated study drug levels is on going.

ALT-801 Phase 2 Trial for Bladder Cancer: An IND has been accepted by the U.S. FDA to initiate a Phase 1b/2 trial of ALT-801 in combination with cisplatin and gemcitabine to treat muscle-invasive or metastatic urothelial cancer (<http://www.clinicaltrials.gov/NCT01326871>). Patient recruitment to this trial has been initiated.

ALT-801 Phase 2 Trials for Other Cancer Indications: Phase 2 trials are also being planned that will further evaluate the efficacy and safety of ALT-801 treatment in an expanded population of patients with prostate cancer, head & neck cancer and renal cell carcinoma. These indications were selected because melanoma and renal cell carcinoma are approved for IL-2 treatment, and patients with each of these cancer types showed some evidence of clinical benefit in the completed Phase 1/2a trial. The MTD level of ALT-801 defined in the current Phase 1b/2 trials will be used for prostate cancer, head & neck cancer and renal cell carcinoma trials. Preclinical efficacy studies are currently underway to evaluate the activity of ALT-801 in combination with chemotherapies commonly used in these cancer types.

A \$3 MM NCI-SBIR Bridge grant has been awarded to Altor to help fund the Phase II ALT-801 clinical trials and Altor was named as a "Success Story" by the Small Business Innovative Research program of the NIH/NCI ([NCI-SBIR Success Stories](#)).

ALT-801 for donor lymphocyte infusion: Altor has an ongoing Phase I clinical trial that will employ ALT-801 as a substitute for IL-2 in NK cell-based donor lymphocyte infusion studies in patients with acute myeloid leukemia (AML). Altor has obtained an approved IND for this approach in collaboration with MD Anderson Cancer Center, Houston. Under MD Anderson's current protocols, lymphocyte cells are obtained from a donor, activated *in vitro* with IL-2, and then transferred into a patient, where the activated lymphocytes show antitumor activity in some patients. The trial will use ALT-801 as a targeted IL-2 agent for the activation of NK cells prior to adoptive transfer into refractory AML patients that have been preconditioned to facilitate cell engraftment. Following NK cell transfer, the patients will also receive 8 doses of ALT-801 to promote targeting of the NK cells against the tumor cells. Clinical response assessment will include the determination of AML blasts present in peripheral blood and bone marrow, time to progression and overall survival and the rate at which patients receiving this regimen are able to go to transplant and the time-to-transplantation.

Altor is seeking a partner that will license, complete clinical development and commercialize this product.

The following non-confidential information can be provided and sent as e-mail attachments:

1. Publications:
 - Wen, J., X. Zhu, B. Liu, L. You, L. Kong, H. I. Lee, K. P. Han, J. L. Wong, P. R. Rhode, and H. C. Wong. 2008. Targeting activity of a TCR/IL-2 fusion protein against established tumors. *Cancer Immunol Immunother* 57:1781.
 - Belmont, H. J., S. Price-Schiavi, B. Liu, K. F. Card, H. I. Lee, K. P. Han, J. Wen, S. Tang, X. Zhu, J. Merrill, P. A. Chavillaz, J. L. Wong, P. R. Rhode, and H. C. Wong. 2006. Potent antitumor activity of a tumor-specific soluble TCR/IL-2 fusion protein. *Clin Immunol* 121:29.
 - Card, K. F., S. A. Price-Schiavi, B. Liu, E. Thomson, E. Nieves, H. Belmont, J. Builes, J. A. Jiao, J. Hernandez, J. Weidanz, L. Sherman, J. L. Francis, A. Amirkhosravi, and H. C. Wong. 2004. A soluble single-chain T-cell receptor IL-2 fusion protein retains MHC-restricted peptide specificity and IL-2 bioactivity. *Cancer Immunol Immunother* 53:345.
2. Altor White Papers relating to:
 - p53 as a target
 - STAR-Ck Technology
 - STAR-Ck Mechanism of Action
 - STAR Diagnostics
3. Keystone Symposia Poster presented in 2009 on interim analysis of ALT-801 Phase I/IIa clinical study.

For more information, contact Altor BioScience Corporation at (954) 443-8600, ext. 832 or e-mail deantaylor@altorbioscience.com. More detailed documentation can be provided upon execution of a confidentiality agreement.