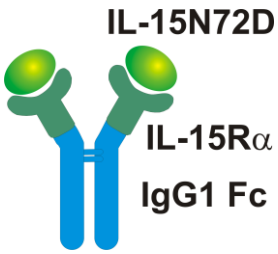
Altor BioScience CORPORATION

**ALT-803 (IL-15 Superagonist Complex)**

**FACT SHEET**

ALT-803 is an investigational agent and has not been approved by regulatory agencies




# ALT-803

**Background**: Interleukin-15 (IL-15) is a critical factor for the development, proliferation and activation of effector natural killer (NK) cells and $CD8^+$ memory T cells. In preclinical studies, this cytokine exhibits potent antitumor activities against well-established tumors in laboratory animal models (Steel, *et al*. 2012). There are several limitations in the development of IL-15-based approaches that include difficulties in producing the clinical product by standard mammalian cell production methods and the short *in vivo* half-life of IL-15. Altor's scientists have overcome these difficulties by developing a novel IL-15 mutant (N72D) with enhanced IL-15 biological activity (Zhu *et al*. 2009). This IL-15N72D mutant and the soluble domain of IL-15Rα was found to form stable heterodimeric complexes in solution and this complex exhibits increased biological activity compared to the non-complexed IL-15. Thus, Altor's scientists constructed a high-yield recombinant mammalian cell line to co-express IL-15N72D and IL-15RαSu/Fc fusion protein as a stable soluble complex. This IL-15N72D:IL-15RαSu/Fc soluble complex is designated as ALT-803.

**Clinical Development of ALT-803:** ALT-803 is Altor's lead IL-15 superagonist product candidate in clinical trials for solid tumors, hematological malignancies and HIV.

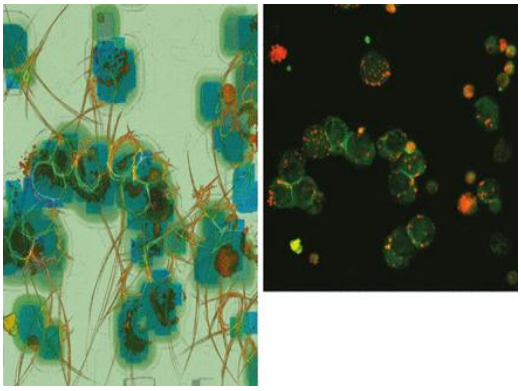
| Phase | Investigational Therapy | Trial Number | Trial Description |
|---|---|---|---|
| I | ALT-803 | NCT01946789 | A Phase 1 Study of the Clinical and Immunologic Effects of ALT-803 in Patients With Advanced Solid Tumors |
| I | ALT-803 | NCT02099539 | A Study of ALT-803 in Patients With Relapsed or Refractory Multiple Myeloma |
| I | ALT-803 | NCT01885897 | IL-15 Super Agonist ALT-803 to Treat Relapse Of Hematologic Malignancy After Allogeneic SCT |
| II | ALT-803 + BCG | NCT02138734 | A Study of Intravesical Bacillus Calmette-Guerin (BCG) in Combination With ALT-803 in Patients With Non-Muscle Invasive Bladder Cancer |
| I | ALT-803 + nivolumab | NCT02523469 | ALT-803 Plus Nivolumab in Patients With Pretreated, Advanced or Metastatic Non-Small Cell Lung Cancer |
| I | ALT-803 + rituximab | NCT02384954 | ALT-803 in Patients With Relapse/Refractory Indolent B Cell Non-Hodgkin Lymphoma (iNHL) in Conjunction With Rituximab |
| I | ALT-803 + gemcitabine + Nab-paclitaxel | NCT02559674 | ALT-803 in Patients With Advanced Pancreatic Cancer Conjunction With Gemcitabine and Nab-Paclitaxel |
| I | ALT-803 | NCT02191098 | Proof of Principle Study of Pulse Dosing of IL-15 to Deplete the Reservoir in HIV Infected People (ALT-803) |

**Potency against Solid and Hematological Tumors in Preclinical Studies:** In various solid and hematological tumor models, ALT-803 exhibits impressive, durable anti-tumor activity as a monotherapy using a weekly dosing regimen. Myeloma bearing mice that were cured after ALT-803 treatment were also highly resistant to re-challenge with the same tumor cells indicating that ALT-803 induces effective immunological memory responses against the tumor cells. ALT-803's novel mechanism of action (MOA) against tumors was discovered by Altor's scientists using two syngeneic multiple myeloma murine models (Xu W *et al*., Cancer Res., 2013). ALT-803 was found to induce $CD8^+$ memory T cells to proliferate, upregulate their innate receptors and produce high levels of IFN-γ (Wong HC *et al.,* Oncoimmunology, 2013). This unique MOA of ALT-803 promotes robust and antigen-independent activity in various tumor models and will likely enhance the efficacy in combination with other cancer drugs against solid tumors and hematological malignancies (Gomes-Giacoia E *et al*., PLoS One., 2014; Mathios D *et al.*, Int J Cancer, 2016). Altor has demonstrated that ALT-803 can indeed synergistically enhance the ADCC activity of therapeutic antibodies and anti-tumor activities of checkpoint inhibitors, such as anti-PD-1, anti-PD-L1 and anti-CTLA antibodies, in relevant preclinical models for various indications (Rhode PR *et al*., Cancer Immunol Res., 2016).

**Efficacy against Infectious Diseases:** Through collaborations with multiple leading research institutions, Altor is also evaluating ALT-803 for treatment of viral infections or as a vaccine adjuvant. In preclinical HIV models, we have demonstrated that ALT-803 can be utilized as a potent HIV-1 latency-reversing agent (Jones RB et al., PLoS Pathog., 2016) and also mediated inhibition of acute HIV-1 infection by activating NK cells (Seay K et al., J Virol., 2015). Thus, Altor is exploring the potential for ALT-803 as a promising immunotherapeutic in HIV eradication approaches.


**About the cover:**

**Artistic rendering & original micrograph shows $CD8^+$ T cells binding and internalizing ALT-803**



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Rhode PR, et al. *Cancer Immunol Res*. 2016 Jan;4(1):49-60.

**Publications:**


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More detailed documentation on ALT-803 may be provided under a confidentiality agreement.


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