Background\ns\n
*NG-796A is a vector encoding a single chain variant form of the human interleukin (IL)-12, IL-15, a soluble form of the Sushi domain of IL-15 receptor alpha (IL-15Rα), and the chemokine CCL21. Locally produced IL-12 and IL-15 cytokines can synergize to drive T- and NK cell activity within the tumor microenvironment (TME) to promote an effective anti-tumor immunity. Dendritic cells can be recruited by the CCL21 gradient to enhance the uptake and presentation of tumor antigens.*

Methods\ns\n
*Transgenes were placed under the control of the virus major late promoter (MLP) which is activated following initiation of genome replication in permissive epithelial tumor cells. Tumor cell lines and primary cells derived from surgically-excised patient tumor samples were infected to evaluate the production and activities of the different transgenes. Further functional experiments were run with peripheral blood derived T-cells and NK cells from healthy volunteers. In vivo data were obtained in a model of immunodeficient mice bearing human tumor xenografts, and adoptively transferred with tumor antigen specific CAR-T cells.*

Results\ns\n
*High levels of functionally active IL-12, as well as the other three transgenes, were produced by *in vitro* infected tumor cells. Interestingly, our initial screening of vectors demonstrated that an effective secretion of IL-15 requires co-expression of the Sushi domain of IL-15Rα. In NG-796A-infected tumor cells co-cultured with T-cells and NK cells, as well as in primary human tumor cell cultures, sustained IL-12 and IL-15 transgene production synergized potently to drive IFNγ production. In *in vitro* transwell-migration assays, CCL21 produced by NG-796A selectively increased the chemotaxis of dendritic cells. Results obtained using human A549 tumor xenografts in immunodeficient mice, showed that intravenous dosing with NG-796A synergized with adoptively transferred tumor antigen specific CAR-T cells to induce long-term clearance of the tumor mass (an effect not observed in mice dosed with EnAd with or without CAR T-cells). This data is consistent with the encoded transgenes supporting the infiltration and anti-tumor activity of T-cells in this solid tumor setting.*

Conclusions\ns\n
*Due to its potential to reprogram the TME and support T-cell activity, NG-796A was selected as a candidate for progression into formal preclinical development activities in preparation for clinical evaluation.*