

Scientific Abstract of Protocol AGS-004-003

Argos Therapeutics, Inc., (Argos) a biotech start-up company co-founded by 2007 Lasker Awardee Ralph Steinman, PhD, is developing AGS-004, an investigational cellular therapy based on proprietary technology (Arcelis™) for ribonucleic acid (RNA)-electroporated dendritic cells (DCs) for human immunodeficiency virus (HIV)-1 infection therapy. Arcelis™ uses DCs generated from each subject's own peripheral blood mononuclear cells (PBMCs) that are matured with "inflammatory mediators" and then electroporated with autologous HIV-1 RNA (Gag, Vpr, Rev, and Nef) amplified from each subject's specific HIV virus. The DCs are also co-electroporated with cluster of differentiation 40 ligand (CD40L) RNA. CD40 protein is expressed by DCs, and CD40/CD40L ligation is required for full maturation of DCs.

Argos has an open IND (Number 13,793) for the Argos HIV clinical program; and AGS-004 has been evaluated in two clinical studies: Protocol CAN-HIV-001¹ and Protocol AGS-004-001.² Protocol CAN-HIV-001, a pilot study (Phase 1/2) testing the immunologic activity and safety of AGS-004 in HIV-infected adults on antiretroviral therapy (ART), was the first-in-man study of AGS-004. Ten subjects were enrolled and completed this study. No drug related adverse events (AEs) of greater than Grade 1 toxicity were observed. Events considered possibly or probably related to AGS-004 treatment were reported in 6 subjects and consisted of mild diarrhea, axillary pain, influenza (flu)-like illness, injection site reactions, fatigue, headache, and rheumatoid factor (RF) increased. No viral blips or clinically relevant changes in CD4⁺ and CD8⁺ T cell counts were observed. The immunology data demonstrated that full (greater than two-fold above baseline) or partial HIV-specific proliferative responses occurred in 7 of 9 evaluable subjects. These responses were specific for the HIV antigens presented by AGS-004 and preferentially targeted the CD8⁺ rather than the CD4⁺ T cell compartment.^{3,4}

Protocol AGS-004-001 is an ongoing Phase 2A study of the safety and antiviral activity of AGS-004 in HIV-infected adult subjects with virologic suppression on ART followed by a planned interruption of ART (analytical treatment interruption [ATI]). The 12-week ATI consists of a well-controlled discontinuation of ART over a planned period of 12 weeks in order to assess whether the viral load (VL) will remain suppressed as a result of AGS-004 treatment. AGS-004 is continued during the ATI to maintain effective antigen presentation of HIV antigens in the face of rebounding virus. The study has been closed to recruitment with an enrollment of 29 subjects as of December 2009. The primary objective of Protocol AGS-004-001 is to assess the ability of AGS-004 therapy to improve immune control of HIV-1 replication, as measured by the proportion of subjects with HIV-1 RNA levels of <1000 copies/mL on at least three time points after ART interruption. The secondary objectives of this study are the evaluation of the safety and tolerability of AGS-004, the effects of AGS-004 on the viral set point, the feasibility of manufacturing AGS-004, and an evaluation of the immunogenicity and mechanism of action. During the course of the study, all (100%) subjects have experienced at least 1 AE and at least 1 AE related to treatment with AGS-004. Eleven subjects (46%) have experienced an AE of at least moderate severity of whom 3 subjects (12.5%) have experienced an AE graded as at least severe. No subjects have experienced Grade 3 or 4 AEs or serious adverse events (SAEs) that were related to treatment with AGS-004, and no subjects have reported an AE leading to the discontinuation of study drug.²²

The proposed study, Protocol AGS-004-003, "A Randomized, Double Blind, Phase 2B Study Testing the Efficacy and Safety of AGS-004 on Host Control of HIV Replication during

Analytical Treatment Interruption,” is based on the hypothesis that AGS-004, when compared to placebo, will decrease the new VL set point established at the end of an ATI. The anti-HIV-1 effects of AGS-004 will accordingly be compared to placebo in a randomized study design. The primary objective is to compare, versus placebo, the anti-HIV effects of AGS 004 as measured by the new plasma HIV VL set point established at the end of the 12-week ATI. The secondary objectives include evaluation of the safety and tolerability of AGS-004; change in HIV VL from pre-ART to the end of ATI; changes in CD4⁺ T cell counts; assessment of plasma VL kinetics; evaluation of immunogenicity; and assessment of inflammatory markers, viral reservoirs, and sequence diversity. The duration of the proposed study is up to 52 weeks in the treatment period with up to 48 weeks of safety follow-up.⁵

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- ¹ A Pilot Study (Phase 1/2) Testing the Immunologic Activity and Safety of AGS-004, an Autologous HIV Immunotherapeutic, in HIV-Infected Adults on HAART. McGill University Health Centre Protocol CAN-HIV-001 (Argos Therapeutics, Inc., Protocol AGS-004-002), Amendment 02 dated 11 December 2006.
 - ² A Phase II Study Testing the Activity and Safety of AGS-004 as an Immunotherapeutic in Successfully ART-Treated Subjects Infected with HIV-1 in Combination with ART Followed by ART Interruption. Argos Therapeutics, Inc., Protocol AGS-004-001, Amendment 02 dated 19 January 2009.
 - ³ Clinical Study Report for Protocol CAN-HIV-001, “A Pilot Study (Phase 1/2) Testing the Immunologic Activity and Safety of AGS-004, an Autologous HIV Immunotherapeutic, in HIV-Infected Adults on HAART.” Argos Therapeutics, Inc., 31 August 2009.
 - ⁴ Routy JP, Boulassel MR, Yassine-Diab B, et al. Immunologic activity and safety of autologous HIV RNA-electroporated dendritic cells in HIV-1 infected patients receiving antiretroviral therapy. Clin Immunol 2009; in press.
 - ⁵ A Randomized, Double Blind, Phase 2B Study Testing the Efficacy and Safety of AGS-004 on Host Control of HIV Replication during Analytical Treatment Interruption. Argos Therapeutics, Inc., Protocol AGS-004-003 dated 14 December 2009.