A NOVEL LYMPHOABLATION PRECONDITIONING AGENT (AVM0703) VIA RECEPTOR MEDIATED INDUCTION OF APOPTOSIS TO REDUCE PATIENT TOXICITIES PRIOR TO CART THERAPY OR STEM CELL TRANSPLANTS TO REDUCE TOXICITIES AND IMPROVE PATIENT SAFETY

Chemotherapy preconditioning prior to CART cells has been strongly associated with CRS, neurotoxicity, patient death and in some instances, has led to clinical trials being put on hold. There is an urgent need to develop a non-toxic and safe agent that lympho-ablates similar to chemotherapy. AVM0703 lympho-ablates both T and B lymphocytes for ‘immune reset’ via receptor mediated induction of caspase dependent apoptosis, sparing neutrophils, platelets, RBCs and stem cells. AVM0703 preconditioning will expand the number of patients eligible for CART therapy to include those too frail to tolerate chemotherapy preconditioning and will reduce the toxicities both medical and financial of chemotherapy or biologics based lymphoablation. HSC based gene therapy holds promise as a cure for many inherited primary immune deficiencies such as sickle cell disease, cerebral adrenoleukodystrophy, cystinosis, epidermolysis bullosa, hemophilia, enzyme replacements disorders, cystic fibrosis and muscular dystrophies. The toxicities of required chemotherapy preconditioning limit the number of people who choose HSCGT. A rela-
tively non-toxic lymphoablating small molecule such as AVM0703 will expand the opportunity for HSCGT. Spontaneous lymphocyte recovery is observed within 14 days. AVM0703 enhances the efficacy of autologous concentrated intra-articular bone marrow injections to treat knee arthritis, accelerates G-CSF-mediated mobilization of HSC into peripheral blood and dramatically enhances CART efficacy against melanoma. AVM0703 is being developed as a replacement for chemotherapy preconditioning (PC) required before allogeneic stem cell transplant (allo Tx), Autologous Hematopoietic Stem Cell Based Gene Therapy (AHSCGT) or Adoptive Cell Therapy (ACT). AVM0703 is being developed as a stand-alone treatment for direct apoptotic killing of relapsed/refractory lymphocytic leukemia, lymphoma and multiple myeloma and for residual HIV and steroid-resistant GvHD.