Study Title	Conditions	Interventions
A Safety and Efficacy Study of TALEN and CRISPR/Cas9 in the Treatment of HPV-related Cervical Intraepithelial Neoplasia Ⅰ	Human Papillomavirus-Related Malignant Neoplasm	Biological: TALEN Biological: CRISPR/Cas9
HPV persistent infection is the major causal factor of cervical intraepithelial neoplasia (CIN) and cervical cancer. The important roles of E6 and E7 playing in HPV-driven carcinogenesis make them attractive targets for therapeutic interventions. Previous evidences showed that using designated TALEN and CRISPR/Cas9 as genome editing tool could produce disruption of HPV16 and HPV18 E6/E7 DNA, significantly decreasing the expression of E6/E7, inducing cell apoptosis and inhibiting cell lines growth. This study will evaluate the safety and efficacy of TALEN-HPV E6/E7 and CRISPR/Cas9-HPV E6/E7 in treating HPV Persistency and HPV-related Cervical Intraepithelial Neoplasia Ⅰ		
Safety of Transplantation ofCRISPR CCR5 Modified CD34+ Cells in HIV-infected Subjects With Hematological Malignances	HIV-1-infection	Genetic: CCR5 gene modification
The investigators performed this study to evaluate the safety and feasibility of transplantation with CRISPR/Cas9 CCR5 gene modified CD34+ hematopoietic stem/progenitor cells for patients that develop AIDS and hematological malignances. Patients will be treated with antiviral therapy (ART) to achieve undetectable HIV-1 virus in peripheral blood before conditioning. CD34+ cells from donors will be infused into the patients after treatment with CRISPR/Cas9 to ablate CCR5 gene.		
Examining the Knowledge, Attitudes, and Beliefs of Sickle Cell Disease Patients, Parents of Patients With Sickle Cell Disease, and Providers Towards the Integration of CRISPR in Clinical Care	Sickle Cell Disease	
Sickle cell disease (SCD) is caused by a genetic defect that affects how hemoglobin is made. Due to this, people with SCD have abnormally-shaped red blood cells, which can result in poor oxygen transport in the body and increase risk of blood clots. CRISPR Cas9 is a new tool which allows scientists to snip and edit genes in a way that is faster, cheaper, and more precise than other gene-editing tools. Recently, research has been done using CRISPR Cas9 to correct the sickle cell gene in animal models and human cells. Researchers want to understand the views of those with SCD, parents of people with SCD, and the providers of these patients regarding use of CRISPR Cas9 in clinical trials and treatment.		
NY-ESO-1-redirected CRISPR(TCRendo and PD1) Edited T Cells (NYCE T Cells)	Multiple Myeloma	Biological: NY-ESO-1 redirected autologous T cells with **CRISPR**edited endogenous TCR and PD-1
This is a first-in-human trial proposed to test HLA-A*0201 restricted NY-ESO-1 redirected T cells with edited endogenous T cell receptor and PD-1. NY-ESO-1 redirected autologous T cells with CRISPR edited endogenous TCR and PD-1 Autologous T cells transduced with a lentiviral vector to express NY-ESO-1 and electroporated with CRISPR guide RNA to disrupt expression of endogenous TCRα, TCRβ and PD-1 (NYCE T Cells).		
Study of CRISPR-Cas9 Mediated PD-1 and TCR Gene-knocked Out Mesothelin-directed CAR-T Cells in Patients With Mesothelin Positive Multiple Solid Tumors.	Solid Tumor, Adult	Biological: anti-mesothelin CAR-T cells
Study of People With Metastatic Gastrointestinal Epithelial Cancer Administering Tumor-Infiltrating Lymphocytes in Which the Gene Encoding CISH Was Inactivated Using theCRISPR/Cas9 System	Gastrointestinal Epithelial Cancer	Drug: Cyclophosphamide Drug: Fludarabine
The gene CISH can weaken immune cells called lymphocytes. It is found in all cells of the body but it most negatively impacts lymphocytes. This study may help people with certain cancers.Lymphocyte cells will be taken from their tumors, the CISH gene will be removed from those cells, then the cells will be returned to the person. Researchers hope this process will help the cells work better and fight the tumors. : A Phase I/II Trial in Patients With Metastatic Gastrointestinal Epithelial Cancer Administering Tumor-Infiltrating Lymphocytes in Which the Gene Encoding CISH Was Inactivated Using the CRISPR/Cas9 System		
A Safety and Efficacy Study Evaluating CTX001 in Subjects With Transfusion-Dependent β-Thalassemia	Beta-Thalassemia Thalassemia	Biological: CTX001
This is a single-arm, open-label, multi-site, single-dose Phase 1/2 study in up to 12 subjects 18 to 35 years of age with transfusion-dependent β-thalassemia (TDT), non-β0/β0. The study will evaluate the safety and efficacy of autologous CRISPR-Cas9 Modified CD34+ Human Hematopoietic Stem and Progenitor Cells (hHSPCs) using CTX001.　CTX001 (autologous CD34+ hHSPCs modified with CRISPR-Cas9 at the erythroid lineage-specific enhancer of the BCL11A gene). Subjects will receive a single infusion of CTX001 through a central venous catheter.		
A Safety and Efficacy Study Evaluating CTX001 in Subjects With Severe Sickle Cell Disease	Sickle Cell Disease	Biological: CTX001
This is a single-arm, open-label, multi-site, single-dose Phase 1/2 study in up to 12 subjects 18 to 35 years of age with severe sickle cell disease (SCD). The study will evaluate the safety and efficacy of autologous CRISPR-Cas9 Modified CD34+ Human Hematopoietic Stem and Progenitor Cells (hHSPCs) using CTX001. A Phase 1/2 Study to Evaluate the Safety and Efficacy of a Single Dose of Autologous CRISPR-Cas9 Modified CD34+ Human Hematopoietic Stem and Progenitor Cells (CTX001) in Subjects With Severe Sickle Cell Disease		
iHSCs With the Gene Correction of HBB Intervent Subjests With β-thalassemia Mutations	Thalassemia	Biological: iHSCs treatment group
This is a single centre、single arm、open-label study, to investigate the safety and efficacy of the gene correction of HBB in patient-specific iHSCs using CRISPR/Cas9. A Safety and Efficacy Study of a Single Center, Open-label, Single Arm About the Gene Correction of HBB in Patient-specific iHSCs Using CRISPR/Cas9 That Intervent Subjests With β-thalassemia Mutations		

Study Title	Conditions	Interventions	
Identification of Host Factors of Norovirus Infections in Mini-Gut Model	Gastrointestinal Infection	Procedure: Duodenal biopsy	非該当
The primary objective in this study is to establish a list of host cellular proteins that mediate norovirus infection. Norovirus is one of the most common pathogens attributed to diarrheal diseases from unsafe food. It is also the primary cause of mortality among young children and adults in foodborne infections. Norovirus is not just a foodborne burden. In a recent meta-analysis, norovirus accounts for nearly one-fifth of all causes of (including person-to-person transmission) acute gastroenteritis in both sporadic and outbreak settings and affects all age groups. Undoubtedly, norovirus is of paramount public health concern in both developed and developing countries. Research efforts to better understand norovirus pathobiology will be necessary for targeted intervention. From Middle East respiratory syndrome coronavirus to Zika virus, efforts to identify host factors important for mediating virus infection has always been a research priority. Such information will shed light on potential therapeutic targets in antiviral intervention. Norovirus virus-host interaction studies have been hampered by the lack of a robust cell culture model in the past 20 years. In 2016, norovirus has finally been successfully cultivated in a stem cell-derived three-dimensional human gut-like structure called enteroid or mini-gut. In this study, intestinal stem cells will be isolated from duodenal biopsies collected from participants, followed by differentiation into mini-guts. Genome-wide genetic screening for host essential and restrictive factors will be performed on infected mini-guts by knockout CRISPR and gain-of-function CRISPR SAM, respectively. Shortlisted candidates will undergo preliminary functional validation in cell lines. These data will provide insights into potential therapeutic targets against norovirus infection.			
Study of PD-1 Gene-knocked Out Mesothelin-directed CAR-T Cells With the Conditioning of PC in Mesothelin Positive Multiple Solid Tumors	Solid Tumor, Adult	Biological: Mesothelin-directed CAR-T cells	
Multiple solid tumors have positive targets of mesothelin expressed on the surfaces of the tumor cells, the investigators use the technique of CRISPR-Cas9 to knocked out the PD-1 of the chimeric antigen receptor (CAR) T cells with the combination of Pretreatment by Paclitaxel and Cyclophosphamideto to effect the immuno-microenvironment around tumors.			
A Study Evaluating UCART019 in Patients With Relapsed or Refractory CD19+ Leukemia and Lymphoma	B Cell Leukemia	Biological: UCART019	
Autologous T cells engineered to express chimeric antigen receptors (CARs) against leukemia antigens such as CD19 on B cells have shown promising results for the treatment of relapsed or refractory B-cell malignancies. However, a subset of cancer patients especially heavily pretreated cancer patients could be unable to receive this highly active therapy because of failed expansion. Moreover, it is still a challenge to manufacture an effective therapeutic product for infant cancer patients due to their small blood volume. On the other hand, the inherent characters of autologous CAR-T cell therapy including personalized autologous T cell manufacturing and widely "distributed" approach result in the difficulty of industrialization of autologous CAR-T cell therapy. Universal CD19-specific CAR-T cell(UCART019),derived from one or more healthy unrelated donors but could avoid graft-versus-host-disease (GVHD) and minimize their immunogenicity, is undoubtedly an alternative option to address above-mentioned issues. We have generated gene-disrupted allogeneic CD19-directed BBζ CAR-T cells (termed UCART019) by combining the lentiviral delivery of CAR and CRISPR RNA electroporation to disrupt endogenous TCR and B2M genes simultaneously and will test whether it can evade host-mediated immunity and deliver antileukemic effects without GVHD.			
Lavage of the Uterine Cavity for Diagnosis of Ovarian Cancer	High Grade Ovarian Serous Adenocarcinoma	Other: Biospecimen Collection	非該当
The goal of this project is to develop a minimally invasive test to detect ovarian cancer, by searching for mutations from the tumor in samples obtained from the cervix (Pap smears), and from the uterus (uterine lavage) in women with advanced ovarian cancer. The investigators plan a pilot study of 25 women with advanced ovarian cancer. Pap smear and uterine lavage samples will be collected while the woman is under anesthesia for planned debulking surgery. A novel, highly sensitive and accurate technique, Crispr-Duplex sequencing, will be used to detect tumor associated mutations in TP53 (the most commonly mutated gene in ovarian cancer) within these samples. These results will be compared to sequencing results in the tumor itself for comparison, and Pap and uterine lavage will be compared to each other to determine the optimal test. Ultimately, the goal is to use the results of this study to plan a larger study including women without cancer who are at either increased risk or normal risk of ovarian cancer, for use in early detection.			
PD-1 Knockout Engineered T Cells for Advanced Esophageal Cancer	Esophageal Cancer	Other: PD-1 Knockout T Cells	
This study will evaluate the safety of PD-1 knockout engineered T cells in treating advanced esophageal cancer. Blood samples will also be collected for research purposes. Peripheral blood lymphocytes will be collected and Programmed cell death protein 1(PD-1) gene will be knocked out by CRISPR Cas9 in the laboratory (PD-1 Knockout T cells). The lymphocytes will be selected and expanded ex vivo and infused back into patients. To avoid allergic reactions, 50 mg hydrocortisone was intramuscularly injected into patient 30 min before cells infusion every time. Best supportive care was also provided for patients.			
Stem Cells in NF1 Patients With Tumors of the Central Nervous System	Neurofibromatosis Type 1	Diagnostic Test: Collection of Stem Cells	非該当
Objectives 1. Establish an induced pluripotent stem cell (iPSC) bank for phenotypically well-characterized patients with NF1. 2. Develop isogenic NF1 wild-type (NF1+/+), NF1 heterozygous (NF1+/-) and NF1 homozygous (NF1-/-) iPSC lines from individual patients using CRISPR/CAS9 technology. 3. Differentiate and characterize disease-relevant brain cells such as excitatory and inhibitory neurons, astrocytes and oligodendrocytes from patient-specific iPSC lines. 4. Screen and identify the drug(s) that can reverse or alleviate the disease phenotypes.			
A Feasibility and Safety Study of Universal Dual Specificity CD19 and CD20 or CD22 CAR-T Cell Immunotherapy for Relapsed or Refractory Leukemia and Lymphoma	B Cell Leukemia	Biological: Universal Dual Specificity CD19 and CD20 or CD22 CAR-T Cells	
CD19-directed CAR-T cell therapy has shown promising results for the treatment of relapsed or refractory B-cell malignancies; however, a subset of patients relapse due to the loss of CD19 in tumor cells. Dual Specificity CD19 and CD20 or CD22 CAR-T cells can recognize and kill the CD19 negative malignant cells through recognition of CD20 or CD22. This is a phase 1/2 study designed to determine the safety of the allogenic gene-edited dual specificity CD19 and CD20 or CD22 CAR-T cells and the feasibility of making enough to treat patients with relapsed or refractory hematological malignancies.			

Study Title	Conditions	Interventions
First-time-in-human (FTIH) Study of GSK3145095 Alone and in Combination With Other Anticancer Agents in Adults With Advanced Solid Tumors	Neoplasms, Pancreatic	Drug: GSK3145095
In an unbiased CRISPR screen, RIPK1 was identified as a top gene contributing to immunotherapy resistance. In addition, RIPK1 has been reported to drive pancreatic oncogenesis. In murine models, inhibition of RIPK1 kinase activity in the pancreatic tumor microenvironment leads to the replacement of tumor-permissive myeloid infiltrates with innate cells that promote an effective antitumor response by adaptive cells. The investigators hypothesize that inhibition of RIPK1 in human pancreatic cancer subjects will modulate the immune infiltrate to sensitize tumors to checkpoint blockade.		
Cell Therapy for High Risk T-Cell Malignancies Using CD7-Specific CAR Expressed On Autologous T Cells	T-cell Acute Lymphoblastic Leukemia	Genetic: CD7.CAR/28zeta CAR T cells
In the laboratory, investigators have also found that T cells work better if they also add proteins that stimulate T cells, such as one called CD28. Adding the CD28 makes the cells grow better and last longer in the body, thus giving the cells a better chance of killing the leukemia or lymphoma cells. Finally, to make sure the T cells are able to grow and expand properly without accidentally targeting themselves (because they also have CD7 on their surface), investigators have removed the CD7 gene in the T cells using a genome editing technique called CRISPR-Cas9. Investigators have repeatedly shown in the laboratory and in our animal studies that removing the CD7 genes in T cells using CRISPR-Cas9 before adding the CAR to the cells helps them expand and kill better, and does not interfere with the other functions of the T cells.		
PD-1 Knockout Engineered T Cells for Muscle-invasive Bladder Cancer	Invasive Bladder Cancer Stage IV	Biological: PD-1 Knockout T Cells
his study will evaluate the safety of PD-1 knockout engineered T cells in treating metastatic advanced bladder cancer. Blood samples will also be collected for research purposes. Peripheral blood lymphocytes will be collected and Programmed cell death protein 1(PDCD1) gene will be knocked out by CRISPR Cas9 in the laboratory (PD-1 Knockout T cells). The lymphocytes will be selected and expanded ex vivo and infused back into patients. Cyclophosphamide at 20mg/kg single dose will be administered 3 days i.v. before cell infusion. A total of 2 x 10^7/kg PD-1 Knockout T cells will be infused in one cycle. Each cycle is divided into three administrations, with 20% infused in the first administration, 30% in the second, and the remaining 50% in the third.Interleukin-2 (IL-2) will be given in the following 5 days, 720000 international unit(IU)/Kg/day (if tolerant). Patients will receive a total of 2, 3, 4 cycles of treatment.		
PD-1 Knockout Engineered T Cells for Castration Resistant Prostate Cancer	Hormone Refractory Prostate Cancer	Biological: PD-1 Knockout T Cells
Peripheral blood lymphocytes will be collected and Programmed cell death protein 1(PDCD1) gene will be knocked out by CRISPR Cas9 in the laboratory (PD-1 Knockout T cells). The lymphocytes will be selected and expanded ex vivo and infused back into patients. Cyclophosphamide at 20mg/kg single dose will be administered 3 days i.v. before cell infusion. A total of 2 x 10^7/kg PD-1 Knockout T cells will be infused in one cycle. Each cycle is divided into three administrations, with 20% infused in the first administration, 30% in the second, and the remaining 50% in the third.Interleukin-2 (IL-2) will be given in the following 5 days, 720000 international unit(IU)/Kg/ day (if tolerant). Patients will receive a total of 2, 3, 4 cycles of treatment.		
PD-1 Knockout Engineered T Cells for Metastatic Renal Cell Carcinoma.	Metastatic Renal Cell Carcinoma	Biological: PD-1 Knockout T Cells
Peripheral blood lymphocytes will be collected and Programmed cell death protein 1(PDCD1) gene will be knocked out by CRISPR Cas9 in the laboratory (PD-1 Knockout T cells). The lymphocytes will be selected and expanded ex vivo and infused back into patients. Cyclophosphamide at 20mg/kg single dose will be administered 3 days i.v. before cell infusion. A total of 2 x 10^7/kg PD-1 Knockout T cells will be infused in one cycle. Each cycle is divided into three administrations, with 20% infused in the first administration, 30% in the second, and the remaining 50% in the third.Interleukin-2 (IL-2) will be given in the following 5 days, 720000 international unit(IU)/Kg/ day (if tolerant). Patients will receive a total of 2, 3, 4 cycles of treatment		
PD-1 Knockout Engineered T Cells for Metastatic Non-small Cell Lung Cancer	Metastatic Non-small Cell Lung Cancer	Drug: Cyclophosphamide
PD-1 Knockout EBV-CTLs for Advanced Stage Epstein-Barr Virus (EBV) Associated Malignancies	Stage IV Gastric Carcinoma	Drug: Fludarabine
Malignant Hyperthermia Registry and Genetic Testing	Malignant Hyperthermia	
The purpose of this study is to to determine the penetrance of known and probable pathogenic variants in genes and the factors that contribute to penetrance in a population of children and adults in the United States exposed to Malignant Hyperthermia (MH) trigger agents. Induced pluripotent stem cells will be differentiated into skeletal muscle cells and functional testing of the ryanodine receptor will be performed. In addition, gene editing using CRISPR technology will be performed to edit/delete variants of uncertain significance.		

Study Title	Conditions	Interventions
Study of Molecular-targeted Therapy Using Zinc Finger Nuclease in Cervical Precancerous Lesions	Human Papillomavirus-Related Malignant Neoplasm	Biological: ZFN-603 and ZFN-758
This research study is being carried out to study a new way to possibly treat human cervical intraepithelial neoplasia (CIN) without invasion. Persistent infection with specific types of human papillomavirus (HPV, most frequently types 16 and 18) may lead to precancerous lesions(CIN). If untreated, these lesions may progress to cervical cancer within many years. In the infected cells, HPV expresses the oncoproteins E6 and E7, both of which play key roles in maintaining viral infection and promoting carcinogenesis. Previous studies has demonstrated that E7 alone, but not E6, is sufficient to immortalize human keratinocytes in vitro and induce high-grade cervical dysplasia in a transgenic mouse model. These data indicated that E7 may dominate the malignant progress in HPV-infected cells. The agents zinc finger nucleases (ZFNs), called ZFN-603 and ZFN-758, which can cleave the HPV16 and HPV18 E7 oncogene specifically. ZFN-mediated disruption of HPV16 and HPV18 E7 DNA directly decreased the expression of E7, induced type-specific apoptosis in HPV16- and HPV18-positive cells, and inhibited cell growth. The purpose of this study is to determine whether ZFN-603 and ZFN-758 are effective in the treatment of HPV16- and HPV18-positive cervical intraepithelial neoplasia.		
A Phase I Study of T-Cells Genetically Modified at the CCR5 Gene by Zinc Finger Nucleases SB-728mR in HIV-Infected Patients	Human Immunodeficiency Virus (HIV)	Drug: ZFN Modified CD4+ T Cells
This is a triple cohort, open-label pilot study of the safety and antiviral activity of a single infusion of autologous CD4+ T cells genetically modified at the CCR5 gene by Zinc Finger Nucleases SB-728mR (ZFN Modified CD4+ T Cells) using electroporated mRNA with or without the prior administration of two different doses of cyclophosphamide.		
Ascending Dose Study of Genome Editing by Zinc Finger Nuclease Therapeutic SB-FIX in Subjects With Severe Hemophilia B	Hemophilia B	Biological: SB-FIX
The purpose of the study is to evaluate the safety, tolerability and effect on FIX antigen and activity levels of ascending doses of SB-FIX. SB-FIX is an intravenously delivered Zinc Finger Nuclease (ZFN) Therapeutic for genome editing. It inserts a correct copy of the Factor 9 gene into the albumin locus in hepatocytes with the goal of lifelong therapeutic production of the Factor IX clotting factor.		
CCR5-modified CD4+ T Cells for HIV Infection	HIV Infections	Biological: SB-728-T Biological: Expanded unmodified autologous CD4+ T cells
A Comparative Study of Autologous CD4+ T Cells Genetically Modified at the CCR5 Gene by Zinc Finger Nucleases SB-728 versus ex vivo Expanded Unmodified Autologous CD4+ T Cells in Treated HIV-1 Infected Subjects Autologous CD4+ T cells with ex vivo modification of the CCR5 gene by zinc finger nucleases		
Ascending Dose Study of Genome Editing by the Zinc Finger Nuclease (ZFN) Therapeutic SB-318 in Subjects With MPS I	MPS I	Biological: SB-318
The purpose of the study is to evaluate the safety, tolerability of ascending doses of SB-318. SB-318 is an intravenously delivered Zinc Finger Nuclease (ZFN) Therapeutic for genome editing. It inserts a correct copy of the α-L-iduronidase (IDUA) gene into the Albumin locus in hepatocytes with the goal of lifelong therapeutic production of the IDUA enzyme. A Phase I, Multicenter, Open-label, Single-dose, Dose-ranging Study to Assess the Safety and Tolerability of SB-318, a rAAV2/6-based Gene Transfer in Subjects With Mucopolysaccharidosis I (MPS I)		
Autologous T-Cells Genetically Modified at the CCR5 Gene byZinc Finger Nucleases SB-728 for HIV	HIV	Biological: ZFN modified T cells
This research study is being carried out to study a new way to possibly treat HIV. This agent is called a "Zinc Finger Nuclease" or ZFN for short. ZFNs are proteins that can delete another protein named CCR5. This CCR5 protein is required for certain common types of HIV (CCR5 tropic) to enter into and infect T-cells. T-cells are one of the white blood cells used by the body to fight HIV. The most important T-cells are those called "CD4 T-cells."		
Study of Autologous T-cells Genetically Modified at the CCR5 Gene by Zinc Finger Nucleases in HIV-Infected Subjects	HIV	Biological: SB-728-T
This research study is being carried out to study a new way to possibly treat human immunodeficiency virus (HIV). The agent is called SB-728-T which are CD4+ T-cells obtained from an individual that are genetically modified at the CCR5 gene by Zinc Finger Nucleases. The CCR5 gene is required for certain types of HIV to enter into and infect T-cells. T cells are one of the white blood cells used by the body to fight HIV. The most important of these are called "CD4+ T-cells" Some people are born without the CCR5 gene on their T-Cells. These people remain healthy and are resistant to infection with HIV. Other people have a low number of CCR5 genes on their T-cells and their HIV disease is less severe and is slower to cause disease (AIDS). The purpose of this research study is to find out whether SB-728-T is safe to give to humans and find out how this affects HIV.		
Phase 1 Dose Escalation Study of Autologous T-cells Genetically Modified at the CCR5 Gene by Zinc Finger Nucleases in HIV-Infected Patients	HIV Infection	Genetic: SB-728-T
This research study is being carried out to study a new way to possibly treat HIV. This agent is called a "Zinc Finger Nuclease" or ZFN for short. ZFNs are proteins that can delete another protein named CCR5. This CCR5 protein is required for certain types of HIV (CCR5 tropic) to enter into and infect your T-cells. T cells are one of the white blood cells used by the body to fight HIV. The most important of these are called "CD4 T-cells." Some People are born without CCR5 on their T-cells. These people remain healthy and are resistant to infection with HIV. Other people have a low number of CCR5 on their T-cells, and their HIV disease is less severe and is slower to cause disease (AIDS). Even with no detectable levels of HIV in the blood, HIV remains in some tissues in the body, primarily the gut tissue. HIV infects the CD4+ T-cells including in the blood and gut. The new treatment to be studied will involve removing white blood cell from the blood that contains CD4+ T-cells. The extracted CD4+ T-cells are then genetically modified by the ZFNs to be resistant to infection by HIV by removing the CCR5 gene from the surface of the CD4+ T cell where HIV enters the cell. Additional genetically modified cells are manufactured and then re-infused back into you. Researchers hope that these genetically modified cells will be resistant to infection by HIV and will be able to reproduce additional resistant CD4+ T-cells in your body. Laboratory studies have shown that when CD4+ T-cells are modified with ZFNs, HIV is prevented from killing the CD4+ T-cells. On the basis of these laboratory results, thre is the potential that ZFNs may work in humans infected with HIV and improve their immune system by allowing their CD4+ T-cells to survive longer. The purpose of this research study is to find out whether "zinc finger" modified CD4+ T-cells are safe to give to humans and find how "zinc finger" modified T-cell affects HIV.		

Study Title	Conditions	Interventions
Safety Study of Zinc Finger Nuclease CCR5-modified Hematopoietic Stem/Progenitor Cells in HIV-1 Infected Patients	HIV	Genetic: SB-728mR-HSPC Infusion 3 days following busulfan conditioning
A Pilot Study to Evaluate the Feasibility, Safety and Engraftment of Zinc Finger Nuclease (ZFN) CCR5 Modified CD34+ Hematopoietic Stem/Progenitor Cells (SB-728mR-HSPC) in HIV-1 (R5) Infected Patients		
Ascending Dose Study of Genome Editing by the Zinc Finger Nuclease (ZFN) Therapeutic SB-913 in Subjects With MPS II	Mucopolysaccharidosis II	Biological: SB-913
The purpose of the study is to evaluate the safety, tolerability and effect on leukocyte and plasma Iduronate 2-Sulfatase (IDS) enzyme activity of ascending doses of SB-913. SB-913 is an intravenously delivered Zinc Finger Nuclease (ZFN) Therapeutic for genome editing. It inserts a correct copy of the IDS gene into the Albumin locus in hepatocytes with the goal of lifelong therapeutic production of the IDS enzyme.		
Repeat Doses of SB-728mR-T After Cyclophosphamide Conditioning in HIV-Infected Subjects on HAART	Human Immunodeficiency Virus (HIV)	Genetic: SB-728mR-T
The purpose of this study is to evaluate the safety and tolerability of repeat doses of T-cell immunotherapy (SB-728mR-T) following cyclophosphamide conditioning. CCR5 is a major co-receptor for HIV entry into T-cells. Disruption of CCR5 by zinc finger nuclease (SB-728mR), blocks HIV entry into the T-cells, therefore, protects the T-cells from HIV infection. Safety (primary outcome) and anti-viral effect (secondary outcome) of zinc finger nuclease-mediated CCR5 disrupted autologous T-cells (SB-728mR-T) will be evaluated in the study.		
CAR + C34 + ZFN -Modified T Cells in HIV Therapy	Hiv	Biological: CD4 CAR+C34-CXCR4+CCR5 ZFN T-cells
This research study is being carried out to study a new way to possibly treat HIV. As part of this study, doctors will take some of your own white blood cells, called T-cells, and modify them so that they can identify and target your HIV cells. The purpose of the study is to evaluate the safety of these modified T cells and determine whether they have any effect on HIV infection. A Pilot Study of T Cells Genetically Modified by Zinc Finger Nucleases SB-728mR, C34-peptide Conjugated to the CXCR4 N-terminus, and CD4 Chimeric Antigen Receptor in HIV-infected Subjects		
A Study to Assess the Safety, Tolerability, and Efficacy of ST-400 for Treatment of Transfusion-Dependent Beta-thalassemia (TDT)	Transfusion Dependent Beta-thalassemia	Genetic: ST-400 Investigational product
This is a single-arm, multi-site, single-dose, Phase 1/2 study to assess ST-400 in 6 subjects with transfusion-dependent β -thalassemia (TDT) who are ≥18 and ≤40 years of age. ST-400 is a type of investigational therapy that consists of gene edited cells. ST-400 is composed of the patient's own blood stem cells which are genetically modified in the laboratory using Sangamo's zinc finger nuclease (ZFN) technology to disrupt a precise and specific sequence of the enhancer of the BCL11A gene (which normally suppresses fetal hemoglobin production in erythrocytes). This process is intended to boost fetal hemoglobin (HbF), which can substitute for reduced or absent adult (defective) hemoglobin, and is done without the use of integrating viral vectors. ST-400 is then infused back into the patient after receiving conditioning chemotherapy to make room for the new cells in the bone marrow, with the aim of producing new erythrocytes with increased amounts of HbF. The primary objective is to understand safety and tolerability of ST-400, and secondary objectives are to assess the effects on HbF levels and transfusion requirements.		
A Study to Assess the Safety, Tolerability, and Efficacy of BIVV003 for Autologous Hematopoietic Stem Cell Transplantation in Patients With Severe Sickle Cell Disease	Sickle Cell Disease	Biological: Plerixafor
Participants will receive plerixafor as subcutaneous (SQ) administration followed by myeloablative conditioning therapy with intravenous (IV) busulfan. BIVV003 will then be administered as a 1-time IV infusion of autologous Cluster of Differentiation 34 + Hematopoietic Stem/Progenitor Cell (CD34+HSPC) transfected ex vivo with zinc finger nuclease (ZFN) messenger ribonucleic acid (mRNAs) targeting the B-cell lymphoma/leukemia 11A (BCL11A) locus.		
Study of Targeted Therapy Using Transcription Activator-like Effector Nucleases in Cervical Precancerous Lesions	Human Papillomavirus-Related Malignant Neoplasm	Biological: T27
Persistent infection with high-risk human papillomavirus (HPVs),especially types 16 and 18,may lead to cervical intraepithelial neoplasia(CIN).HPVs expresses the oncoproteins E6 and E7, both of which play key roles in maintaining viral infection and promoting carcinogenesis. Previous studies showed that using designated TALENs (T27 and T512) targeted HPV16 E6 and E7 produced disruption of HPV16 E6 and E7 DNA, decreased the expression of E6 and E7 proteins, and induced cell apoptosis. This study will evaluate the safety and efficacy of T27 and T512 in treating HPV Persistency and HPV16-positive CIN. T27 suppository contain 500 μg of T27 and suppocire. Other Name: TALEN-T27		