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| **Protocol ID:**  | **Protocol Director:**  |

1. Please review the FDA guidance for long term follow-up after administration of human gene therapy products (<https://www.fda.gov/media/113768/download>) and describe the plan for long term follow-up (or state N/A if no follow-up). Include information on:
	1. whether long-term follow-up will occur as part of the current protocol or as a separate protocol;
	2. the purpose and duration of long-term follow-up observations;
	3. the time intervals;
	4. the locations at which you plan to request the subjects to have scheduled study visits or be contacted by other means; and
	5. details as to what those contacts will involve.

(also include the above information in consent forms)

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1. State pre-existing patient conditions that may amplify the risks of using this vector or gene transfer product or state there are none (e.g., products reactivating Epstein Barr virus (EBV), cytomegalovirus (CMV), herpes zoster virus (HZV),Hepatitis B virus (HBV), etc.). If there are conditions that may amplify risks, describe exclusions or considerations for eligibility and how participants will be prescreened, and applicable risk information (also add exclusions to eProtocol Section 8h, add risks in eProtocol section 9a, and add risks to consent forms).

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1. Is there any possibility that an autopsy may be requested (e.g., to test vector persistence, transgene expression, or related adverse reactions)? **yes** [ ]  **no** [ ] .
If yes, confirm [ ]  that this language or similar language is in the procedures section of your consent forms:
*Gene Transfer Studies*

*If you participate in this study, the research doctor may ask your family for permission to perform an autopsy if you pass away while the study is still in follow up. An autopsy may help researchers learn more about [XYZ]. Because the decision about performing an autopsy would be up to your family, we encourage you to advise them of your wishes. Your family would not be responsible for the costs of the autopsy.*

1. Confirm [ ]  that consent forms state the approximate number of people who have previously received the study product/genetic material under study.
2. Is this is a first in human study? **yes** [ ]  **no** [ ]

If yes, please confirm [ ]  the first page of the consent form includes a statement that the study is a first in human study. We also suggest that you include a statement explaining how the purpose of a phase 1 study is not to provide treatment. Sample language below (please revise based on specifics of your study).

*This is the first study with the study product where it is being given to humans. This phase 1 study is designed mainly to test toxicity and other harmful effects of the study product in humans at different doses. Although we will collect information about how well the study product works at treating your condition, treatment is not the primary aim of a phase 1 study. While it is possible that this study product may provide some benefit in treating your disease, it is unknown at this time if it will provide any benefit.*

1. Is this is a dose escalation study where some participants may be receiving a dose that is sub-therapeutic or toxic? **yes** [ ]  **no** [ ]

If so, please confirm [ ]  that the risk section of your consent form includes a statement about how the dose they receive may not be effective at treating their condition or may be toxic.

1. If the study product does not meet specified release criteria, will it still be infused into study participants? **yes** [ ]  **no** [ ]  If yes, please address the following:

1. Describe the process of evaluating the product to determine if it can still be infused and the approvals you will obtain prior to infusing an out of specification product (e.g., sponsor, FDA, Data and Safety Monitoring Committee, IRB).

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1. Describe the parameters that will be used to determine the minimum product release criteria. If you cannot provide specifics, please provide us with the categories and a range of parameters if possible (e.g., will not infuse product with endotoxins, mycoplasma, Replication Competent Lentivirus, visible particles of plastics or other contaminates, will not infuse a product with less than a XYZ cell dose, etc.).

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1. The consent form must contain a description of any reasonably foreseeable risks or discomforts for the participants. Please confirm [ ]  the consent form contains a lay description of how the study product may not meet specified release criteria and what risks are associated with using the non-confirming product.

1. Are you testing for [communicable diseases](https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ReportableDiseases.pdf) (e.g., COVID-19, HIV, HCV, TB) specifically for this research study? **yes** [ ]  **no** [ ]
2. If yes, confirm [ ]  that researchers included a statement in consent forms that positive results will be reported to health authorities:
*You will be tested for communicable diseases [list which: COVID, HIV, HCV, etc.] as part of this research study. If your test results are positive, the results will be reported to health authorities as required by law.*
3. If you are you testing for HIV confirm [ ]  that researchers included this statement in consent form(s):
*If you test positive for HIV, counseling will be provided.*

1. Are you requesting the short form consent process for possibility of encountering non-English speaking participants? **yes** [ ]  **no** [ ]
	1. If yes, confirm [ ]  that application includes the Short Form Process in section 13 and an Alteration of HIPAA Authorization in section 15.
	2. If yes, is this a study involving an investigational biologic, drug, and/or device? **yes** [ ]  **no** [ ]
		1. If yes, confirm [ ]  that the complete consent form will be translated after the short form is used, submitted to the IRB for review, and will be provided to the participant after approval.
2. Confirm [ ]  that the risks section of consent forms includes a statement about any risks for becoming pregnant, getting a partner pregnant, or risks to reproductive capabilities if known. Or, if there is no information about these risks, confirm [ ]  that a statement like this or similar in the risk section is included:
*If you are pregnant or currently breast feeding, you should not participate in this study. This study may involve risks to an embryo, fetus, or nursing infant that are currently unknown. It is also unknown if the study product may damage sperm or be present in seminal fluid.*
3. Does your study involve pregnancy testing and minors? **yes** [ ]  **no** [ ]
If yes, please note that there are California minor consent laws that impact how pregnancy results can be communicated. Please confirm [ ]  that researchers included this language to consent and assent forms:
For the parent/guardian consent form:
*As part of this study, pregnancy testing will be performed. The results of pregnancy tests for those under 18 are confidential according to California Minor Consent Laws. If you are a parent whose child is participating in this study, results will be given to your child by one of the study nurses or doctors in private. Every effort will be made to maintain confidentiality regarding positive pregnancy test results. Although we will not typically tell parent(s) or guardian(s) without your child's permission, under certain circumstances, we might be compelled to reveal this information. For example, if your child's life or someone else's life is at risk or if abuse is suspected, it may be necessary to inform you as parent(s) or guardian(s) of a positive pregnancy test. If we believe it is necessary to tell a parent or guardian of a positive pregnancy test without your child's permission, we will meet with your child first in private to discuss our concerns before divulging any information regarding pregnancy. During research, if your child has a positive pregnancy test, we may withdraw your child from the study. This means that even if we do not reveal the results, you may suspect that your child is pregnant despite our best efforts to maintain confidentiality. If your child becomes pregnant or if there is any chance that your child is pregnant (late menstrual period), please contact the study personnel immediately so that we may provide medical assistance and counseling.*
For the minor assent form:
*If you have had your first period: (Include this header if one assent form will be used for younger and older children) During the research, pregnancy testing will be performed. The results of the pregnancy tests will be told to you by one of the study nurses or doctors in private. Every effort will be made to keep positive pregnancy test results a secret. Although we will not typically tell your parent(s) or guardian(s) without your permission, there may be times we might need to reveal this information. For example, if your life or someone else's life was at risk or if abuse was suspected, it may be necessary to tell your parent(s) or guardian(s) of a positive pregnancy test. If we believe it's necessary to tell your parent or guardian of a positive pregnancy test without your permission, we would meet with you first in private to discuss our concerns prior to giving any information to your parent(s) or guardian(s) regarding pregnancy. During the research, if you do have a positive pregnancy test, we may remove you from the study. This means that even if we do not reveal the results, your parent(s) or guardian(s), may suspect that you are pregnant despite our best efforts to keep the information secret. If you become pregnant or if there is any chance that you might be pregnant (late period, broken condom, missed oral birth control pills, etc.) please contact the study personnel immediately so that we may provide medical assistance and counseling.*
4. Will specimens be obtained for this research and used for whole genome sequencing? **yes** [ ]  **no** [ ]
If yes, confirm [ ]  include this statement as applicable: *The process of determining all or nearly all of your DNA sequence is called whole genome sequencing. It is different from genetic testing that does not involve whole genome sequencing because it provides a much more detailed snapshot of your genome. This research (will/might/will not) include whole genome sequencing.*
5. Will samples in the study will be used for genetic testing or future research on samples will include genetic testing? **yes** [ ]  **no** [ ]
If yes, please confirm [ ]  that researchers included this language to consent forms:
*Genetic Testing and Future Research
As part of the analysis on your specimens, the investigators (may/will) do genetic testing. Genetic research is research that studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications and responses to treatment. Genetic research raises certain questions about informing you of any results. Possible risks of knowing results include: anxiety; other psychological distress; and the possibility of insurance and job discrimination. A possible risk of not knowing includes being unaware of the need for treatment. These risks can change depending on the results of the research and whether there is a treatment or cure for a particular disease. Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.*(If investigators will not share the research results with the participant, the following language can be added)
*The results of the study of your specimens from this project will be used for research purposes only, and you will not be told the results of the tests.*
(If investigators will allow participants to choose whether they want to receive test results and/or will contact participants in the future, the following language (two choices of language) can be added)
*Regarding informing you of the test results, you should understand the following:*
* *The information may be too limited to give you particular details or consequences;*
* *You may be determined to carry a gene for a particular disease that can be treated;*
* *You may be determined to carry a gene for a particular disease for which there is no current treatment;*
* *You carry a gene for a disease and might consider informing relatives that they, too, might carry the gene.*

(Or)

*Investigators in this study may try to re-contact you in the future. If you are re-contacted and want to know what the investigators have learned about your specimens, you should understand the following:*

* *The information may be too limited to give you particular details or consequences;*
* *You may be determined to carry a gene for a particular disease that can be treated;*
* *You may be determined to carry a gene for a particular disease for which there is no current treatment;*
* *You carry a gene for a disease and might consider informing relatives that they, too, might carry the gene.*
1. Does the trial involve retroviral vectors? **yes** [ ]  **no** [ ]
If yes, confirm [ ]  that researchers included FDA required language as applicable in consent forms (see <https://www.fda.gov/media/113768/download>). If any of the below language has not been included, please explain why:

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-Description of study agent - The study involves giving a person some cells that have been changed by a retroviral vector.  A retroviral vector is a virus that can insert genetic material into cells.

-Mechanism of action for retroviral vectors - When retroviral vectors enter a normal cell in the body, the deoxyribonucleic acid (DNA) of the vector inserts itself into the normal DNA in that cell. This process is called DNA integration.

-Effect of DNA integration - Most DNA integration is expected to cause no harm to the cell or to the patient.  However, there is a chance that DNA integration might result in abnormal activity of other genes.  In most cases, this effect will have no health consequences.  However, in some cases, abnormal activity of a gene may cause unpredictable harm such as the development of cancer.

-Discussion of delayed adverse event, leukemia-like malignancy, occurring in human studies - It is important that you know about some cancers that occurred in another gene therapy research study. Clinical studies were conducted in France and United Kingdom to treat a disease called X-linked Severe Combined Immunodeficiency (SCID).  Years after receiving cells that were modified by a retroviral vector, a significant number of the children in this small study developed a leukemia-like malignant disease (cancer).  One child died from the cancer.  A group of experts in this field studied the results from tests performed on these children’s blood cells.  They concluded that cancer was caused by the retroviral vector DNA. Still, most of the children with X-linked SCID who have received experimental gene therapy have not been found to have cancer at this time.  Although they appear healthy, we still do not know whether they, too, will develop cancer.

-Risk of malignancy for this study - We do not know if the retroviral vector used in this protocol might cause cancer.  However, you should be aware that the DNA contained in retroviral vectors will integrate into your DNA and that under some circumstances; this has been known to cause cancer months to years later.