CEDARS-SINAI MEDICAL CENTER

CONSENT FORM FOR RESEARCH

TITLE: HUMAN NEURAL PROGENITOR CELLS EXPRESSING GLIAL CELL LINE-DERIVED NEUROTROPHIC FACTOR (CNS10-NPC^{GDNF}) FOR THE TREATMENT OF ALS

STUDY SUPPORT PROVIDED BY: **CALIFORNIA INSTITUTE OF REGENERATIVE MEDICINE**

PARTICIPATING RESEARCHERS:

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STUDY CONTACT PHONE NUMBER AT CSMC: 424-315-2694

AFTER HOURS CONTACT (24 HOURS): 310-423-6472

This research study is funded by a grant from the California Institute of Regenerative Medicine (CIRM) and is an investigator initiated study. CIRM only reimburses Cedars-Sinai Medical Center for the costs associated with running the study; CIRM is not providing additional compensation to Cedars Sinai Medical Center or the Principal Investigator for their participation in the study. Clive Svendsen PhD is the sponsor of the Investigational New Drug (IND) under which this study is being performed.

1. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

We are doing this study to examine the safety and effectiveness of the stereotactic drug delivery device and the safety of transplanting cells that have been genetically engineered to produce a growth factor into the spinal cord of patients with Amyotrophic Lateral Sclerosis (ALS) to see if these cells help protect the motor neuron cells that are damaged in patients with ALS. The cells are called *neural progenitor cells,* which are a type of stem cell that can become several different types of cells in the nervous system. A growth factor is a substance that is required for the stimulation of growth in living cells. The growth factor in the cells used in this study is called *glial cell line-derived neurotrophic factor,* or GDNF. GDNF is a protein that promotes the survival of many types of neuronal cells. Therefore, the cells are called "CNS10-NPC-GDNF."

You are being asked to take part in this research study because you have been diagnosed with amyotrophic lateral sclerosis (ALS), with symptoms present for less than 3 years. As the study requires frequent visits for follow-up, you and your caregiver must be able to make the necessary trips to the medical center.

The study will enroll up to 25 people in total.

This research study is designed to test the investigational use of CNS10-NPC-GDNF cells. These cells have not been approved by the U.S. Food and Drug Administration (FDA).

The investigational cells have been tested in animals, but have not yet been tested in people. In this study, we want to learn:
• the safety of delivering CNS10-NPC-GDNF cells into the spinal cords of people.
• which dose of the cells is safe to use in people.

Two different doses of the study drug will be given. The first nine study participants will receive the lowest dose. If the drug does not cause serious side effects, it will be given to other nine study participants at a higher dose. You will be notified which dosing group you are in. Between the first 3 subjects on each dose level, a minimum of 4 weeks will be waited before giving the dose to the next subject for safety. Additionally, a minimum of 4 weeks will be waited between the first dose and the second increased dose. Then the study will be completed. You will not receive additional doses of the drug.

The surgical procedure for placing these cells in the spinal cord requires the use of specially designed surgical tools and equipment. The device is called the "Sterotactic Surgical System." This new device was developed at Cedars and is experimental, meaning it is not approved by the U.S. Food and Drug Administration (FDA). They will be used in the operation to deliver/inject the cells.

Although there are other research studies that use similar cell products and devices, this is the first time that these particular cells and the new surgical device will be used in people. This study is designed to see if the surgical procedure and the cell product are safe.

2. WHAT WILL HAPPEN DURING THE STUDY?

This section provides a general overview of what will happen during your participation in this study. Information included below should be considered along with the flowchart of procedures attached as Appendix A.

The flowchart shows a timeline for research-related procedures that are involved in your participation in this study. **Research-related procedures** are those performed solely for the research. They would not be performed if you did not take part in the study.

A table describing common medical procedures done solely for the purposes of monitoring and assessing your condition during this study is attached as Appendix B to the end of this consent form. Standard of care procedures that will be repeated or done at greater frequency are listed in the flow chart, attached Appendix A.

Overview of study:
If you consent to participate in the study, you will undergo preliminary testing to make certain that you are healthy enough to undergo the required surgery, and to evaluate the extent of your ALS. There will also be repeat testing to establish your baseline of some clinical assessments related to ALS, such as testing to determine the strength of various muscles in the leg, and how well your nerves interact with those muscles. This testing is a combination of some routine testing as well as some testing that is not commonly used to evaluate ALS.

After you have completed these screening and baseline procedures, you will have a visit with the neurosurgical team before your surgery to make certain that you are healthy enough to have surgery.

You will be admitted to Cedars-Sinai Medical Center hospital and prepared for surgery on the same day. You will receive a dose of medication through a vein to prevent your immune system from rejecting the transplanted cells. This drug is named 'basiliximab' and it is part of a family of medications called 'immunosuppressants' or 'immunosupressive drugs' that make your immune system less reactive to foreign cells.

You will receive the investigational cell product in a surgery that is expected to last about 5 hours. The CNS10-NPC-GDNF cells will be injected into one side of the area of the lumbar spinal cord in your low back. This area of the spinal cord controls the legs. For the neurosurgeon to reach the spinal cord, it is necessary to do a surgical procedure on the lower back and remove some bone. This surgery is called a laminectomy. A laminectomy is not an experimental surgery. Laminectomies are performed commonly as part of the care of various abnormalities of the spine. It is not a part of the routine care of people who have ALS. The laminectomy will remove approximately 2 inches of bone only from the back of your spine, and will not cause your spine to be unstable.

Cell Product description:
The cells were derived from a tissue sample from a 9-week old fetus provided by University of Klinikum in Germany. The tissue donation was obtained under a research protocol with full consent. The tissue was transferred to University of Wisconsin's clinical bio manufacturing facility for further processing. A lentivirus was used to make the cells secrete growth factor (GDNF) in the spinal cord. The virus was previously altered, and tested, to assure the virus does not grow or spread. The lentivirus is no longer active in the cell, but the FDA requires testing of your blood for Replication Competent Lentivirus (RCL) during the clinical trial to ensure that there is no active lentivirus in your system. A clinical grade cell lot was manufactured and stored for research use (CNS10-NPC-GDNF).

This product was made by genetically modifying a cell line with a virus. When the virus was originally received at the manufacturing facility there was a notification procedure that was not followed by the manufacturer and a committee whose responsibility for employee safety was not made aware that the virus was at the manufacturing facility. The investigational product was manufactured according to approved Standard Operating Procedures (SOPs) and in accordance with Good Manufacturing Procedures. The product passed all release and safety testing. The manufacturing procedure has been audited by and independent third party and found to be adequate. The documentation produced was reviewed by both an independent third party as well as representatives from the Food and Drug Administration (FDA) and found to be satisfactory.

Once the small amount of bone has been removed, the membrane surrounding the spinal cord will be cut to expose the spinal cord. This will allow the neurosurgeon to see your spinal cord and the blood vessels in the area of the surgery. You will be randomized to have either the left or right side of the spinal cord injected. The neurosurgeon can choose to change the randomized side of injection based on the appearance of the blood vessels and other structures The neurosurgery team will be the only people who know which side of your spinal cord has received the investigational treatment. You and all others who will be making the clinical assessments will be 'blinded,' which means that you will not know which side of the spinal cord the cells were implanted in. This will allow for a comparison of

the function and progression of ALS in the leg on the treated side of the spinal cord compared with the leg on the untreated side.

Opening the membrane surrounding the spinal cord is not an experimental procedure. It is commonly used to reach the spinal cord. Following the administration of the CNS10-NPC-GDNF cells, the membrane will be sewn closed.

The CNS10-NPC-GDNF cells will be delivered very slowly via a total of ten injections to separate areas of the spinal cord on the same side.

After all of the cells have been administered, the neurosurgeon will repair and close all openings that were made as part of the procedure. You will be closely monitored until you are ready to be transferred to the Intensive Care Unit for your recovery. You will spend approximately 5-8 days in the hospital. During this time, you will be given standard medications for pain.

The administration of CNS10-NPC-GDNF cells is similar to having an organ transplant, with the exception that a much smaller number of cells are put into your body. As with organ transplants, it will be necessary for you to take medications called 'immunosuppressants' to prevent the body from rejecting the transplanted cells. After surgery, you will begin taking pills that work in different ways to suppress your immune system. You will take these medications for the duration of the study (12 months) unless you have serious side effects. If this happens, the immunosuppressant drugs will be stopped or the dosages may be altered. You will receive a second dose of basiliximab, an FDA-approved immunosuppressant drug, through a vein on or near the fourth day after surgery.

When you are stable and the doctors think it is safe, you will be discharged from the hospital to go home. When you go home, you will have a supply of the immunosuppressive pills that you will continue to take. Follow-up may be more frequent based on the stability of your lab level results of the testing during follow-up.

Beginning one month after the surgery, you will return to the medical center. A variety of tests and examination will take place if you are in this study. These tests are listed in Appendix A. The testing includes lab tests to check how the immunosuppressive drugs are working and whether any adjustments in dosages need to be made, and a general evaluation to see how you are doing and to identify any problems you may be having. Other specific evaluations will measure the progression of your ALS.

A group of scientists and medical doctors will be watching over the study to identify any unexpected risks. They are the Medical Monitor and his specialty specific consultants. This group has the authority to stop the study at any time due to safety concerns. After the participants in the first group have had surgery to administer the CNS10-NPC-GDNF, the Medical Monitor will review all of the safety data to determine whether it is safe for the dose to be increased in the next group of participants. If they determine that the side effects were those that were expected, then they will indicate that the second group can be treated.

It is important to understand that this study involves the transplantation of cells into your spinal cord. After the transplant is done, it is impossible to remove the cells from your body, or to stop the cells from producing the growth factor. At any time before the surgery, you can change you mind and

choose not to participate. However, after the surgery, you will have the cells in your body for the rest of your life. We will closely observe the response to the transplanted cells for the first 12 months, and will monitor your condition for the rest of your life.

Autopsy
The only way to learn if the transplanted cells remain alive would be to remove a part of the spinal cord and study it in a laboratory. As it is not possible to remove a piece of spinal cord without causing harm, we ask you to consider whether you would allow an autopsy after you die, and making your wishes known to your family members. Agreeing to an autopsy is not required to be in the study. You will sign a separate consent form if you agree to have an autopsy performed. The information gained from a study of autopsy tissue will add much knowledge to the field of stem cell transplantation as a potential treatment for ALS.

How long will you be in the study
We think you will be in this study for about 15 months. The total time includes nine study visits. Before surgery, there are three visits for screening, baseline, and pre-surgery evaluations. For the surgery, you will be admitted to the hospital and spend approximately 5-8 days. After surgery, you will return for three monthly visits, then three more visits over a period of 9 months.

We would like to keep track of your medical condition for the rest of your life. We would like to follow you with a vitality status check every 6 months via an in-person clinic visit, phone call, or electronic message exchange. Depending on any medical signs and symptoms you report, you may be asked to undergo a thoracolumbar MRI on an as needed basis if the study investigators feel it is appropriate. Keeping in touch with you and checking on your condition every so often helps us look at long-term effects.

3. WHAT ARE THE POSSIBLE RISKS?

Risks of common medical procedures performed solely for research purposes are described in a table attached to the end of this consent form as Appendix B. Side effects and risks of standard of care procedures are not described in this consent form.

This section describes the possible risks and/or discomforts we anticipate you could experience that are related to the study procedures:

From the surgery and drug delivery system used during surgery:

- Side effects of medications used in spinal surgery, both experimental and not experimental
  - Pain medications: sleepiness, nausea, constipation, difficulty breathing
  - Nausea medications: abnormal movements, headache, dizziness, diarrhea
  - Blood clot prevention medications: bleeding including mild or serious blood loss
  - Muscle relaxants: difficulty breathing, slowing of heartbeat
  - Medications used to treat constipation: abdominal cramps, diarrhea
- Temporary or permanent spinal cord dysfunction: weakness, paralysis, numbness, or difficulty urinating
- Pain around the operative site
- Damage to surrounding soft tissues
- Nausea and vomiting

- Headache, which may be severe and last up to 1 week post-operatively
- Temporary slowing or stopping of normal intestinal movement
- Temporary swelling of the face due to being positioned on the stomach during surgery
- Pain or irritation or infection of the urethra due to indwelling Foley (bladder) catheter
- Infection of skin, near the site of the surgery
- Separation of the edges of the surgical wound that might require additional surgery
- Infection in the blood (bacteremia)
- Urinary tract infection
- Bleeding which cannot be controlled
- Blood clot in a vein in leg or lung
- Permanent spinal cord problems that might include weakness, paralysis, numbness, difficulty urinating, weakness or paralysis of breathing muscles
- Loss of bowel or bladder control which might be permanent
- Changes in sexual functioning which might be permanent
- CSF (cerebral spinal fluid) could leak under the skin (pseudomeningocele) or through the incision
- Death

From the transplant of cells:

- Tumors, possibly brain tumors, spinal cord tumors, or meningeal masses malignant or benign
- Pain caused by changes in sensory nerves.
- The body's immune response to the cells could damage the spinal cord resulting in pain, spasticity (stiffness), weakness, numbness, loss of bowel, sexual or bladder control
- Infection

From the Investigational stereotactic drug delivery device

- *Slippage, dislodgement, or targeting error which may result in misplacement of the cells*
- *Tissue shearing*

From GDNF:

- Neuropathic pain
- Lhermitte's syndrome (electrical sensation that runs down the back and into the limbs)
- Cerebellar purkinje cell loss, in rare cases (the loss of a class of neuronal cells in the brain)

Radiation Risk:

- This research study involves exposure to radiation from a series of Thoracic-Lumbar Spine X-rays and Chest X-rays. This radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation that you will receive from each Thoracic-Lumbar Spine x-ray is approximately 100mRem and from each Chest x-ray is approximately 10mRem. This amount is comparable to about 2% of the total amount that each radiation worker is allowed to receive from radiation usage each year (5,000 mRem). This use involves minimal risk and is necessary to obtain the research information desired. This radiation exposure is not necessary for your medical care and is for research purposes only.

From outcome measurements:
EIM

- Light pressure on the skin during electrode application
- Rare risk of irritation from saline solution used to moisten the skin

CMAP

- Temporary discomfort during nerve stimulation

ATLIS

- Muscle fatigue or cramping

From the immunosuppressive treatment:
The immunosuppression regime used in this study is the common immunosuppression regime prescribed when someone undergoes an organ transplant. Since the cells you will be receiving in this study did not come from you, the investigators believe is necessary to reduce the reaction your immune system may have to the cells by giving medications that suppress the immune system. Standard immunosuppression regime carries significant risks ranging from common/minor risks to very serious risks as detailed in Appendix C. The risks of these specific medications are listed in Appendix C. Every effort will be made to treat the side effects of these medications if possible. Some side effects may require treatment with additional medications including the possibility of insulin injections for high blood sugar. These side effects should subside when the immunosuppression medications are stopped.

The immunosuppression drugs used in this study may increase your risk of certain infections. You may be prescribed an antibiotic, antiviral and/or antifungal medications to prevent infections associated with the immunosuppression regimen. Your study doctor will discuss the risks of these medications should they be prescribed.

Unknown Risks
There also may be other side effects or risks that we cannot predict including risk of exposure to relevant communicable disease agents and diseases. Many side effects may go away shortly after the study medication or procedure is stopped. However, in some cases they can be serious, long-lasting, permanent, and/or fatal.

If you experience any side effects during your participation in the study, you will be treated according to standard medical practice. The risks of any treatments required to address any side effects resulting from the experimental procedures will be reviewed with you by your study doctor.

Reproductive and Lactation Risks
Taking part in this research study can affect an unborn baby. Therefore, you should not become pregnant or father a baby while on this study. If you or your partner is capable of becoming pregnant you will need to use birth control. Check with the researcher about approved birth control methods to use while participating in this study.

Women should not breastfeed a baby while on this study.

Unknown Risks to the Developing Embryo or Fetus (an unborn baby)
If you are pregnant, or become pregnant during participation in this research, the study procedures and treatment might involve risks to an embryo or fetus, which are currently unknown. It is important that you contact the researcher immediately if you believe you might be pregnant.

Follow-up Visit for Discontinuing Participants
While you are free to discontinue your participation at any time, we encourage you to complete a Final Study Visit. During this visit, we will conduct tests to collect safety data, and discuss any information that may be important to share with your treating physician.

Incidental Findings and Duplicate Tests
The procedures in this study are for research purposes and no clinical care or information will be provided to you as part of this study.
It is possible that the study procedures could detect a medical problem that was not the focus of the research and about which you may not already be aware. If we learn that the results of research procedures could suggest information relevant in an important way to your health, we will notify you. We will not provide any specific diagnosis about the information seen during research scans performed at the Research Imaging Core facility, although we may suggest your physician order a particular test or procedure to further investigate the finding. Your primary care physician will determine if it is in your best interest to obtain this test for you. There may be added risks of having further diagnostic tests, and we suggest that you discuss this with your primary care physician.

You will not be provided with information from the screening blood test to check your kidney function other than noting whether your screen met our standards. If not, you will be told and encouraged to discuss this with your primary physician. We will not provide the blood test results to your primary physician.

4. ARE THERE BENEFITS IN TAKING PART IN THE STUDY?

The primary purpose of phase I (or early phase clinical trials such as this) is to study the safety (side effects) of the treatment and to determine the maximum safe dose. Accordingly the primary purpose of this study is not to provide direct benefit to research participants who enroll. Phase I investigational treatment is offered to research participants when no other standard treatment exists or has been determined to be ineffective or when standard treatment has a very low chance of benefit.

You should not expect to benefit from taking part in this research study. We hope the information learned from this research study will benefit other individuals with ALS in the future by helping us to learn whether a combined approach of using stem cells that have been genetically altered to produce a growth factor are safe and should be studied in future clinical studies.

5. WHY WOULD MY PARTICIPATION BE STOPPED?

Your participation in this study may be stopped at any time by the researcher or the sponsor without your consent for any reason, including:
- The study is stopped or suspended;
- Funding for the study is reduced, stopped or withdrawn;
- If it is in your best interest;
- You do not consent to continue in the study after being told of changes in the research that may affect you;
- You do not follow the study procedures.

If your participation in the study is stopped and you do not complete all the scheduled follow-up visits during the first year following the surgical delivery of the cells, we would still like to contact you by

phone to see how you are doing. If you chose to withdraw from this study, you will be asked to come to the medical center for a final safety visit.

6. ARE THERE ANY OTHER OPTIONS?

Your participation is voluntary so you have the right to decline to participate or to withdraw from this research study at any time without any penalty or loss of benefits to which you would be entitled outside of the study. Choosing not to participate will not affect the care you receive at Cedars-Sinai Health System.

If you decide not to take part in this study, you have other choices. For example:

- you may choose to be treated following the usual clinical approach of multidisciplinary supportive ALS care and/or treatment with Riluzole which is the only FDA approved medication for the treatment of ALS.
- you may choose to take part in a different study at CSMC or elsewhere, if one is available
- you could decide not to be treated.

The researcher will discuss these options and their risks and benefits with you.

7. WILL MY INFORMATION BE KEPT CONFIDENTIAL?

We will do our best to make sure that the personal information collected as part of this study is kept private. However, we cannot guarantee total privacy. A copy of your research consent and authorization forms may be filed in your electronic medical record at CSMC. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other identifiable personal information will not be used. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include: accrediting agencies, government and regulatory groups (such as Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), etc.), safety monitors, companies that sponsor the study, and authorized representatives of the sponsor.

You may, depending on the circumstances of the study and applicable law, be asked to sign a separate "Authorization Form" that outlines with whom your information may be shared for the purposes of this research and under what circumstances.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website at any time.

As part of this research, it is necessary to restrict your right to access copies of health information created during your participation in your research while the research study is in progress. This applies only to the surgery report and neurosurgery notes. This restriction is necessary to maintain the blinding, in other words, it is important to the study outcomes that you not know into which treatment group you were assigned. Your right to access this information will be restored upon completion of the study.

8. WHAT IF I BECOME ILL OR INJURED BECAUSE OF TAKING PART IN THIS STUDY?

Contact your researcher at once if you feel that you are ill or have been injured because of taking part in this study. If it is a medical emergency, call 911 or go to an emergency room. Promptly notify your researcher of your situation at the phone number listed on page 1 of this consent form.

Who pays for my research related illness or injury?
A research injury or illness is a direct result of the Study Treatment and/or Devices or a procedure performed only as a part of the study and is not part of your standard clinical medical treatment. Injury or illness related to your underlying medical condition or treatment generally provided outside of the study would not be considered research related. If you are being treated for a research injury or illness, you will not pay for the costs of care provided by Cedars-Sinai Health System or in any emergency room provided that you are being treated for a research injury or illness. Cedars-Sinai may, however, ask for reimbursement where allowed from parties such as your health plan. CSMC has no plans to pay for losses such as lost wages. If you choose to obtain non-emergency care elsewhere, you or your health plan may be responsible for the costs of that care.

9. FINANCIAL CONSIDERATIONS

Costs of Participation
You and your insurance company will not be charged for your participation in this research study. The Sponsor will cover the cost of all items, drugs and services required by this study, including any procedures required by the study that may be standard of care.

Compensation for Participating
You will not be paid for taking part in this research study.

Financial Interest in the Research
CSMC has a financial interest in this study as follows:

- Cedars-Sinai owns the patent application related to the devices being tested in this study.

The PI and institution have no other potential financial conflict of interest with respect to this study.

A significant financial interest is a situation in which financial considerations have the potential to influence a person's professional judgment. This study has been designed to minimize the impact of the investigator's financial interest. You are encouraged to ask the investigator to explain how the financial interest disclosed below will be managed.
Pablo Avalos, a research scientist in Clive Svendsen's laboratory and Doniel Drazin, a neurosurgeon are both named on the patent application related to the device being tested in this study. Therefore, its is possible that they would receive future royalty income under the patent.

10. WHAT IF I HAVE QUESTIONS OR PROBLEMS?

Please contact one of the investigators listed on the first page of this form for questions or concerns about the research.

If you have questions, problems, or concerns that you want to discuss with someone who is not associated with this study, or want to offer suggestions or feedback, please contact:

Cedars-Sinai Human Research Protection Program (HRPP) Phone: (310) 423-3783
Email: ResearchConcerns@cshs.org

The Cedars-Sinai HRPP has been established to protect the rights and welfare of research participants. You may also contact the Cedars-Sinai HRPP if you want to offer input or obtain information regarding the study.

11. CONSENT PROVISIONS

If you sign this form below, it means that:

(1) You have taken the time to carefully read and understand the information presented in this informed consent form; you should discuss it with others, and if appropriate seek a second opinion to make an informed decision;
(2) The information concerning the research study and its involved procedures has been fully explained to you and your questions have been answered to your satisfaction;
(3) You have received and understand all of the information you desire regarding your participation in the research study;
(4) You have considered the potential risks, any anticipated benefits and alternatives (and their relative risks and benefits) of participation;
(5) You are voluntarily agreeing to participate in this research study;
(6) You understand that by consenting to participate in the research, you are not giving up any of your legal rights (other than the postponement of your access to certain health information as described in this informed consent form);
(7) You understand that you have the right to be informed of significant new findings related to this research study which may affect your willingness to continue participating in this study; and
(8) You have been provided with a copy of the "Experimental Subject's Bill of Rights", if applicable to this research study, and have been provided with an opportunity to ask questions regarding the Bill of Rights.

We will give you a copy of this signed and dated consent form and a signed copy of the Experimental Subject's Bill of Rights.

SIGNATURE BY THE PARTICIPANT:

_____	_____	_____
Name of Participant (Print)	Signature of Participant	Date of Signature

SIGNATURE BY THE INVESTIGATOR:

I have personally explained the research to the participant in non-technical terms, answered all questions, and attest that he/she freely consents to participate. The participant has been provided with the Experimental Subject's Bill of Rights.

_____ _____
Signature of the Investigator Who Obtained Consent Date of Signature

SIGNATURE BY THE WITNESS/INTERPRETER

Signature of a witness is required when an English-speaking subject who has been determined to have capacity to consent is unable to read or physically sign the consent form, but choses to indicate via a "mark" or verbally or non-verbally communicate that he/she agrees to participate. The witness signs the consent form to confirm that an oral consent process occurred and that the individual verbally consented to participate in the research.

TO BE MARKED AT TIME OF SIGNATURE:
Consent obtained:

__ From English speaking individual who is not physically able to sign the consent document

_____ _____
Signature of Witness **Date of Signature**

CEDARS-SINAI MEDICAL CENTER

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

In accordance with California Health and Safety Code 24172, **any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:**

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

_____ _____

Signature of Experimental Subject **Date**

Distribution instruction for researchers:

The signed (i) Consent form, (ii) Authorization for Use and Disclosure of Identifiable Health Information and (iii) "Experimental Subject's Bill of Rights" (the latter required if the research study involves medical interventions)* should be distributed to:

1) Medical Chart
2) Research Participant
3) Pharmacy (if a drug study)
4) Principal Investigator's research records (original)

APPENDIX A: FLOWCHART OF PROCEDURES

	Screening	Base-line	Pre Op[1]	Surgery	24hrs. Post Surgery	Mo 1	Mo 2	Mo 3	Mo 6	Mo 9	Mo 12 Final Safety Visit	Q6 Mo
Informed Consent	x											
History/PE	x					x	x	x	x	x	x	
Vital Signs including height and weight	x	x				x	x	x	x	x	x	
Neurological Exam	x					x	x	x	x	x	x	
Hematology/Coags	x					x		x	x	x	x	
Safety Labs/Clinical Chemistry[1]	x					x		x	x	x	x	
Pre-operative screening/Medical Clearance			x									
Serum for GDNF levels	x							x			x	
Electrocardiogram (EKG)			x									
Chest x-ray			x									
Immune Monitoring[2]						x	x	x	x	x	x	
DSA	x							x	x		x	X[3]
Cell administration				x								
Lumbar Puncture -CSF for GDNF levels				x				x			x	
Deep Vein Thrombosis Testing (pre-operative)			x									
ALSFRS-R Score	x	x				x		x	x	x	x	
EIM	x	x				x		x	x	x	x	
CMAP	x	x				x		x	x	x	x	
Force Generation ATLIS	x	x				x		x	x	x	x	
Thoraco-lumbar x-ray	x											
Thoraco-Lumbar MRI	x				X				x		x	
Muscle MRI		x						x	x	x	x	
Forced Vital Capacity/ Maximum Inspiratory Pressure	x	x				x		x	x	x	x	
Urinary bladder assessment (ultrasound)	x					x		x	x	x	x	
Pain Assessments	x	x				x		x	x	x	x	
Single Question QOL	x	x				x		x	x	x	x	
Adverse Events	x	x		x		x	x	x	x	x	x	
Concomitant Medications	x	x		x		x	x	x	x	x	x	
RCL	x							x	x		x	X[3]
Vitality Assessment Phone Call												x
Assessment of investigational cell delivery device (first 5 subjects)				X								

1. Safety labs to include Hematology with differential panel: complete blood count with differential (hematocrit, hemoglobin, platelet count, RBC indices, Total RBC, Total WBC, and WBC & differential). Blood chemistry panel/Liver function tests: alanine aminotransferase (ALT (SGPT)), aspartate aminotransferase (AST (SGOT)), albumin, alkaline phosphatase, bicarbonate, blood urea nitrogen, calcium, chloride, creatinine, glucose, magnesium, phosphate, potassium, sodium, total bilirubin and total protein. Urinalysis: microalbumin, bilirubin, blood, clarity, color, glucose, ketones, nitrate, pH, protein, specific gravity, urobilinogen and WBC screen. Serum human chorionic gonadotrophin (hCG) for WOCBP (collected only at Screening Visit, and as necessary throughout course of study)
2. Immune Monitoring includes trough levels for Tacrolimus, along with GDNF antibody.
3. 3. Replication Competent Lentivirus (RCL) screening samples will be drawn annually after completion of the 12 month follow-up period as per FDA regulations.

APPENDIX B: Detailed Description of Common Medical Procedures Performed for Research Purposes and Associated Risks

The procedures listed below are often performed as part of routine care for a person with your condition. They are being repeated, or performed more frequently as part of this research. However, the risks associated with each procedure should be comparable to what you would experience even if you were undergoing the procedure outside this research study.

Study Procedure	Related Risks
Medical History/Physical Exam: Includes height, weight, vital signs (heart rate and blood pressure). You will be asked about your medical and surgical history. You will be asked about your age, gender, race, ethnicity. This should take approximately 20 minutes.	There are no physical risks associated with these procedures.
Neurological Examination: You will be examined by a neurologist who will assess your mental status, muscle function, sensation, reflexes, coordination, and gait. This exam can take up to 30 minutes.	There are no physical risks associated with these procedures.
Blood draw: A needle is placed in the vein in your arm to draw blood. The blood draw will take approximately 15 minutes.	Blood drawing may cause some pain and has a small risk of bleeding, bruising, or infection at the puncture site. There is also a small risk of fainting.
Lumbar Puncture: Lumbar Puncture (LP) is a standard procedure used in medical practice. You will be asked to lie on your side with your knees pulled up to your abdomen. Your low back will be cleaned and sterilized. You will receive numbing medication to reduce the discomfort of the procedure. A needle will be placed in your low back to draw out the fluid that surrounds your spinal cord. After the procedure, the injection site will be covered with a dressing and you will be asked to lie flat or on your side for approximately one hour. The procedure will take approximately 30 minutes, but you will be in the procedure room for at least 1 ½ hours.	The side effects of an LP may include back discomfort, bleeding, headache, pain at the LP site, and infection. Pain during the LP procedure will be prevented or minimized by using local anesthesia (Lidocaine). Infection after a lumbar puncture is very rare, but serious, and will be treated with antibiotics. Approximately 1 out of 3 people who have a lumbar puncture develop a post-lumbar puncture headache. Post lumbar headaches are more common in females and in people less than 30 years old. This headache can be mild to severe. Occasionally the headache may be severe enough to interfere with your normal daily activities (i.e. work, school, etc.). You will receive medication as needed. If the headache lasts more than 3 days a blood patch may be performed. This procedure involves taking blood from you and injecting it in the same place where the spinal needle was put in during the lumbar puncture. The clotting of the blood in this space should stop further fluid leaking and stop the headache. Nausea, dizziness and ringing in the ears may accompany the headache.
Deep Vein Thrombosis Testing: You will have an ultrasound of the veins in your legs to determine if there is a clot. This will involve	There is a small chance of skin irritation from ultrasound gel. You should not feel any sensation from the ultrasound itself.

having a gel applied to your leg. The ultrasound head will be moved along your skin over the gel to visualize your veins. This test takes approximately 30 minutes.	
ALS Functional Rating Scale –Revised (ALSFRS-R): You will be asked a series of questions about how you are doing with your daily function. This scale takes approximately 5 minutes to complete	If you feel uncomfortable or embarrassed answering any question, you may skip it. The questionnaire will be labeled with a unique study number that will link your identity so that only the research team can recognize you.
Electrical Impedance Myography (EIM): EIM is a measure of muscle health. We will test 4 muscles in each of your legs. Your skin will be moistened with water and then an electrode will be placed over the muscle. Each muscle will be tested twice. This testing will take approximately 10 minutes.	You may feel some coolness when the water is applied to your skin, You will not feel any stimulation from the EIM electrode. Light pressure on the skin during electrode application Rare risk of irritation from saline solution used to moisten the skin
Strength Testing (ATLIS): You will have your strength tested using the ATLIS. The ATLIS will measure how strong your legs muscles are. You will be asked to sit in the ATLIS chair then push and pull against a fixed force. You will be asked to give your full effort for this testing. This test will take approximately 30 minutes to perform.	You many experience shortness of breath during this testing as you are giving your full effort to test your strength. You can rest between each test to catch your breath. You may feel some muscle soreness the day after the testing. These feelings of shortness of breath and muscle soreness are temporary. Muscle fatigue or cramping
Compound Motor Action Potential (CMAP): CMAP is a measure of nerve function. You will have one muscle tested on each leg. An electrode will be placed on your foot and the neurologist will then stimulate the nerve further up your leg. This test will take approximately 10 minutes.	When your nerve is stimulated, you may feel a slight shock type sensation. This feeling is mild and will go away when the stimulation is stopped. Temporary discomfort during nerve stimulation
Magnetic Resonance Imaging (MRI): A MRI is a test that uses a magnetic field and pulses of radio wave energy to make pictures of organs and structures inside the body. During the procedure you will lie down in a large donut-like looking magnet and we will ask you to lie still on a table for the duration of the procedure (about 2 hours). You will be able to communicate with researchers all the time and you will have a panic button to use if you want to stop the procedure at any time. The MRI will take approximately 45 minutes to an hour.	You may feel slightly anxious inside the scanner due to a fear of small enclosed spaces (claustrophobia). Also, at times, you may hear very loud noises as the MRI machine is taking pictures of your body. You may be given headphones and may request ear plugs if you feel the noise is too loud. At any time, you may ask the technician to stop the exam if you are unable to complete the exam. The research MRI's are performed in an area that also performs MRI on animals. **If you are allergic to animal dander, please let the study coordinator know**.
Forced Vital Capacity/Maximum Inspiratory Pressure Testing: Your breathing will be tested to determine your respiratory health. We will place a nose plug on your nose and ask you to take a deep breath in. A sensor filter will be	You may feel lightheaded or slightly short of breath during or just after the breathing test. You will be able to lie down if you are feeling faint. This feeling is temporary and should go away with rest. You may feel discomfort from lying flat for a

placed in your mouth and you will be asked to blow all the air out of your lungs as hard and fast as you can. You will be asked to perform this test at least three times at each visit. Breathing tests will take approximately 15 minutes.	prolonged period of time. You may also experience headache or irritation from scanner noise
Thoraco-Lumbar X-Ray: You will be asked to stand for this test. A radiographic picture will be taken of your thoracic and lumbar spine. You will have this test one time only and it will take approximately 10 minutes.	You will not feel anything during the x-ray procedure. Radiation exposure from an x-ray is low. Some organs are more radiosensitive than others.
Chest X-Ray: Two views of the chest are taken, one from the back and the other from the side of the body as the patient stands against the image recording plate. This test will take approximately 15 minutes.	You will not feel anything during the x-ray procedure. Radiation exposure from an x-ray is low. Some organs are more radiosensitive than others.
Electrocardiogram: abbreviated as EKG or ECG – is a test that measures the electrical activity of the heartbeat using electrodes (disposable adhesive discs placed on the skin).	There's no pain or risk associated with having an electrocardiogram. When the disposable adhesive discs are removed from your skin, there may be some minor skin discomfort or irritation. You may experience temporary discomfort (pulling on the skin/skin hair) during removal of the patches. This hair may be shaved for patch placement.
Urinary Bladder Ultrasound: You will have an ultrasound of your empty bladder to determine if your bladder is able to empty completely. This will involve having a gel applied to your lower abdomen. The ultrasound head will be moved along your skin over the gel to visualize your bladder. This test will take approximately 15 minutes	There is a small chance of skin irritation from ultrasound gel. You should not feel any sensation from the ultrasound itself.
Questionnaires: You will be asked to complete a questionnaire. We will ask you questions to evaluate your quality of life and any pain you may be experiencing. We think it should take about10 minutes to complete the questionnaire. Questionnaires will ask you to respond to questions about any pain you may be having and how you would rate your overall quality of life.	If you feel uncomfortable or embarrassed answering any question, you may skip it. The questionnaire will be labeled with a unique study number that will link your identity so that only the research team can recognize you.
Adverse Event Assessment: You will be asked about any medical or physical changes that may have occurred. Assessment of adverse events will take approximately 15 minutes.	There are no physical risks associated with these procedures.
Concomitant Medications: You will be asked about your previous and current medications that you take. Assessment of concomitant medications will take approximately 15 minutes.	There are no physical risks associated with these procedures.

APPENDIX C: RISKS ASSOCIATED WITH THE IMMUNOSUPPRESSIVE REGIME

Basiliximab

Common, some may be serious (occurs in greater than 20% of people)	**Occasional, some may be serious** (occurs in ≥ 10% of people)	**Possible, some may be serious** (occurs in ≥3-10% of people)	**Rare, and serious** (occurs in less than 2% of people)
• Gastrointestinal Disorders	• Constipation • Nausea • Abdominal pain • Vomiting • Diarrhea • Dyspepsia (indigestion) • Peripheral edema • Fever • Viral infections • Hyperkalemia (high potassium levels) • Hypokalemia (low potassium levels) • Hyperglycemia (high blood sugar) • Hypercholesterolemia (high cholesterol) • Hypophosphatemia (low phosphate levels) • Hyperuricemia (high uric acid) • Urinary tract infection • Dyspnea (shortness of breath) • Upper respiratory tract infection • Surgical wound complications • Acne • Hypertension (high blood pressure) • Headache • Tremor • Insomnia (inability to sleep)	• Accidental trauma • Asthenia (lack of energy) • Chest pain • Increased drug level • Infection • Face edema • Fatigue • Dependent edema • Generalized edema • Leg edema • Malaise (physical discomfort) • Rigors (shaking chills) • Sepsis(illness caused by infection in the body) • Abnormal heart sounds • Aggravated hypertension (high blood pressure) • Cardiac failure • Hypotension (low blood pressure) • Enlarged abdomen • Esophagitis (inflammation of the esophagus) • Flatulence • Gastroenteritis (inflammation of the stomach and intestines) • GI hemorrhage (bleeding in the gastrointestinal tract) • Gum hyperplasia (enlargement of the gums) • Melena (black “tarry” stool) • Moniliasis (yeast infection) • Ulcerative stomatitis (recurrent canker sores) • Arrhythmia (irregular heart beat) • Atrial fibrillation • Tachycardia (rapid heartbeat) • Acidosis (increased acidity in the	• Allergic reaction • Excessive hair growth

		blood) • Dehydration • Diabetes Mellitus • Fluid overload • Hypercalcemia (high levels of calcium) • Hyperlipidemia (high levels of lipids) • Hypertriglyceridemia (high levels of triglycerides in the blood) • Hypocalcemia (low levels of calcium) • Hypoglycemia (low blood sugar) • Hypomagnesaemia (low levels of magnesium in the blood) • Hypoproteinemia (low levels of protein) • Weight increase • Arthralgia (joint pain) • Arthropathy (disease of the joints) • Back pain • Bone fracture • Cramps • Hernia • Myalgia (muscle pain) • Leg pain • Dizziness • Neuropathy • Paresthesia • Hypoesthesia (numbness) • Hematoma (bruising) • Hemorrhage • Purpura (bleeding under the skin) • Thrombocytopenia (low platelet count) • Thrombosis (blood clots) • Agitation • Anxiety • Depression • Polycythemia (producing too many blood cells) • Genital edema • Impotence • Bronchitis • Bronchospasm • Abnormal chest sounds • Coughing • Pharyngitis (sore throat) • Pneumonia	

		• Pulmonary disorder • Pulmonary edema • Rhinitis(stuffy nose) • Sinusitis (inflammation of the nasal sinus) • Cyst • Herpes simplex • Herpes zoster • Hypertrichosis (excessive hair growth) • Pruritus (itching) • Rash • Skin disorder • Skin ulceration • Albuminuria (increased protein in the urine) • Bladder disorder • Dysuria (painful urination) • Frequent micturition (urination) • Hematuria (blood in the urine) • Oliguria (reduced amounts of urine) • Abnormal renal function • Renal tubular necrosis • Ureteral disorder • Urinary retention • Vascular disorder • Cataract • Conjunctivitis (pink eye) • Abnormal vision • Leucopenia (low white blood cells)	

Tacrolimus

Common, some may be serious (occurs in greater than 15% of people)	**Occasional, some may be serious** (occurs in 3-15% of people)	**Possible, some may be serious** (occurs in 1-3% of people)	**Rare, and serious** (occurs in less than 1% of people)
• Tremor • Headache • Insomnia (inability to sleep) • Paresthesia (tingling or pricking sensation) • Dizziness • Diarrhea • Nausea • Constipation	• Abnormal dreams • Agitation • Amnesia • Anxiety • Confusion • Convulsion • Crying • Depression • Elevated mood • Emotional lability	• None	• Serious infection • Lymphomas • Malignancies • Severe allergic reaction

• Vomiting • Dyspepsia (indigestion) • Hypertension (high blood pressure) • Chest pain • Urinary Tract Infection • Hypophosphatemia (low phosphate levels in the blood) • Hypomagnesaemia (low levels of magnesium) • Hyperlipidemia (high levels of lipids in the blood) • Hyperkalemia (high potassium levels) • Diabetes Mellitus • Hypokalemia (low potassium levels) • Hyperglycemia • Edema • Anemia • Leukopenia • Infection • Peripheral edema • Asthenia (lack of energy) • Abdominal pain • Pain • Fever • Back pain • Dyspnea (shortness of breath) • Increased cough • Arthralgia (joint pain) • Rash • Pruritus (itching)	• Encephalopathy • Hemorrhagic stroke • Hallucinations • Hypertonia (low muscle tone) • Incoordination • Monoparesis (weakness in one area) • Myoclonus • Nerve compression • Nervousness • Neuralgia (nerve pain) • Neuropathy • Paralysis flaccid • Impaired psychomotor skills • Quadriparesis (weakness in all limbs) • Somnolence (sleepiness) • Abnormal thinking • Vertigo (dizziness) • Impaired writing • Abnormal vision • Amblyopia (abnormal vision) • Ear pain • Tinnitus (ringing in the ears) • Cholangitis (infection of the biliary tract) • Cholestatic jaundice (yellowing of the skin secondary to blocked bile tract) • Dudodenitis (inflammation of the small intestinal tract • Esophagitis (inflammation of the esophagus • Flatulence • Gastritis • Gastroesophagitis (inflammation of the stomach and esophagus • Gastrointestinal hemorrhage (bleeding in the intestines) • GI disorder • GI perforation • Hepatitis • Ileus (bowel obstruction) • Increased appetite • Jaundice • Liver damage • Esophagitis ulcerative (ulcers in the esophagus) • Oral moniliasis (yeast infection) • Pancreatic pseudocyst		

	• Rectal disorder • Stomatitis (inflammation of the stomach) • Abnormal ECG • Chest pain • Arrhythmia (abnormal heart rate) • Atrial fibrillation • Atrial flutter • Bradycardia (slow heartbeat) • Cardiac fibrillation • Cardiopulmonary failure • Cardiovascular disorder • Congestive heart failure • Deep thrombophlebitis • Heart failure • Decreased heart rate • Hemorrhage • Hypotension (low blood pressure) • Peripheral vascular disorder • Phlebitis • Postural hypotension • Syncope (dizziness) • Tachycardia (rapid heartbeat) • Thrombosis (blood clots) • Vasodilatation (dilatation of the blood vessels) • Acute kidney failure • Albuminuria (albumin in the urine) • Nephropathy • Bladder spasm • Cystitis (inflammation of the bladder) • Dysuria (painful urination) • Hematuria (blood in the urine) • Hydronephrosis (swelling of the kidney) • Kidney failure • Kidney tubular necrosis • Nocturia (awaking at night due to the need to urinate) • Pyuria (pus in the urine) • Toxic nephropathy • Urge incontinence • Urinary frequency • Urinary incontinence • Urinary retention • Vaginitis (inflammation of vagina) • Acidosis (high levels of acid in the body		

	fluids) • Dehydration • Gout • Abnormal healing • Hypercalcemia (high levels of calcium) • Hypercholesterolemia (high cholesterol) • Hypophosphatemia (low phosphate levels) • Hyperuricemia (high levels of uric acid in the blood) • Hypervolemia (fluid overload) • Hypocalcemia (low levels of calcium) • Hypoglycemia (low blood sugar) • Hyponatremia (low levels of sodium in the blood) • Hypoproteinemia (low levels of protein) • Weight gain • Cushing's Syndrome • Coagulation disorder • Ecchymosis (discoloration of the skin) • Abnormal blood values • Hypochromic anemia • Leukocytosis (increased while blood cells in the blood) • Polycythemia (increased hemoglobin in the blood) • Enlarged abdomen • Abscess • Accidental injury • Allergic reaction • Cellulitis (infection of the skin) • Chills • Feeling abnormal • Flu syndrome • Generalized edema • Hernia • Decreased mobility • Peritonitis (inflammation of the lining of the stomach) • Photosensitivity reaction • Sepsis (illness caused by infection in the body) • Temperature intolerance • Ulcer • Arthralgia (joint pain) • Cramps		

	• Generalized spasm • Joint disorder • Leg cramps • Myalgia (muscle pain) • Osteoporosis • Asthma • Emphysema • Hiccups • Lung disorder • Decreased lung function • Pharyngitis (sore throat) • Pneumonia • Pneumothorax (air in the chest cavity) • Pulmonary edema • Respiratory disorder • Rhinitis (stuffy nose) • Sinusitis (inflammation of the nasal sinus) • Voice alteration • Acne • Alopecia (hair loss) • Exfoliative dermatitis (scaly dry skin) • Fungal dermatitis • Herpes simplex • Herpes zoster • Hirsutism (male pattern hair growth in women) • Benign neoplasm skin • Skin discoloration • Skin disorder • Skin ulcer • Sweating		

Mycophenolate Mofetil

Common, some may be serious (occurs in greater than 20% of people)	**Occasional, some may be serious** (occurs in 4-20% of people)	**Possible, some may be serious** (occurs in 1-3% of people)	**Rare, and serious** (occurs in less than 1% of people)
• Pain • Abdominal pain • Fever • Headache • Infection • Sepsis(illness caused by infection in the body) • Asthenia (lack of energy)	• Enlarged abdomen • Abscess • Cellulitis (infection of the skin) • Chills • Cyst • Face edema • Flu syndrome • Hemorrhage	• Severe neutropenia	• Lymphoma • Non-melanoma skin cancer • Other malignancy

• Chest pain • Back pain • Ascites (abdominal swelling secondary to fluid retention) • Anemia (low red blood cells) • Leukopenia (low white blood cells) • Thrombocytopenia (low platelet count) • Hypochromic anemia • Leukocytosis (increased white blood cells) • Urinary tract infection • Abnormal kidney function • Hypertension (high blood pressure) • Hypotension (low blood pressure) • Cardiovascular disorder • Tachycardia (rapid heartbeat) • Peripheral edema • Hypercholesteremia (high cholesterol levels) • Edema • Hypokalemia (low potassium levels • Hyperkalemia (high potassium levels) • Hyperglycemia (low blood sugar) • Hypomagnesaemia (low magnesium levels) • Hypocalcemia (low calcium levels) • Diarrhea • Constipation • Nausea • Dyspepsia (indigestion) • Vomiting • Anorexia • Infection • Dyspnea (shortness of breath) • Increased cough • Lung disorder • Sinusitis (inflammation of the	• Hernia • Malaise (physical discomfort or illness) • Neck pain • Pelvic pain • Peritonitis (inflammation of the lining of the stomach) • Coagulation disorder • Ecchymosis (discoloration of the skin) • Pancytopenia (low red blood cells, white blood cells, and platelets) • Petechia (a small red or purple spot caused by bleeding in the skin) • Polycythemia (producing too many blood cells) • Acute kidney failure • Dysuria (painful urination) • Hydronephrosis (swelling of the kidney) • Hematuria (blood in urine) • Impotence • Kidney tubular necrosis • Nocturia (awaking in the night secondary to the need to urinate) • Oliguria (reduced amount of urine) • Pain • Prostate disorder • Pyelonephritis (urinary tract infection) • Scrotal edema • Urinary frequency • Urinary incontinence • Urinary retention • Urinary tract disorder • Arrhythmia (abnormal heartbeat) • Arterial thrombosis • Atrial fibrillation • Atrial flutter • Bradycardia (slow heartbeat) • Cardiovascular disorder • Congestive heart failure • Heart arrest • Heart failure • Hypotension (low blood pressure)		

nasal sinus) • Pleural effusion (fluid build-up around the lungs) • Rash • Tremor • Insomnia (inability to sleep) • Dizziness • Anxiety • Paresthesia (tingling or prickling sensation)	• Pallor (paleness) • Palpitations • Pericardial effusion • Peripheral vascular disorder • Postural hypotension • Pulmonary hypertension • Syncope (dizziness) • Tachycardia (rapid heartbeat) • Thrombosis (blood clots) • Vasodilation • Vasospasm • Abnormal healing • Acidosis • Generalized edema • Gout • Hypercalcemia (high calcium) • Hypercholesteremia (high cholesterol) • Hyperlipidemia (high lipids in the blood) • Hypovolemia (low blood volume) • Thirst • Weight gain • Weight loss • Anorexia • Cholangitis (infection of the bile duct) • Dysphagia (difficulty swallowing) • Esophagitis (inflammation of the esophagus) • Flatulence • Gastritis • Gastroenteritis (inflammation of the stomach and intestines) • Gastrointestinal disorder • Gastrointestinal hemorrhage • Gingivitis inflammation of the gums) • Hepatitis • Ileus (bowel obstruction) • Infection • Jaundice • Liver damage • Melena (blood in the stool) • Mouth ulcerations		

	• Rectal disorders • Stomach ulcer • Apnea (temporary cessation of breathing) • Asthma • Atelectasis • Bronchitis • Epistaxis (nose bleeds) • Hiccup • Hyperventilation • Lung edema • Lung disorder • Neoplasm (abnormal tissue growth) • Pain • Pharyngitis (sore throat) • Pleural effusion • Pneumonia • Pneumothorax (air in the chest cavity) • Respiratory disorder • Rhinitis (stuffy nose) • Sinusitis (inflammation of the nasal sinus) • Increased sputum • Voice alteration • Acne • Alopecia (hair loss) • Fungal dermatitis • Hirsutism (male pattern hair growth in women) • Pruritus (itching) • Rash • Skin disorder • Sweating • Agitation • Anxiety • Confusion • Convulsion • Delirium • Depression • Dry mouth • Emotional lability • Hallucinations • Hypertonia (high muscle tone)		

	• Hypesthesia (decreased ability to feel) • Nervousness • Neuropathy • Paresthesia (tingling or prickling sensation) • Psychosis • Somnolence (sleepiness) • Abnormal thinking • Vertigo • Arthralgia (joint pain) • Joint disorder • Leg cramps • Myalgia (muscle pain) • Osteoporosis • Abnormal vision • Amblyopia (abnormal vision) • Cataract • Conjunctivitis (pink eye) • Deafness • Ear disorder • Ear pain • Eye hemorrhage • Tinnitus (ringing in the ears)		

Prednisone

Common, some may be serious (occurs in greater than 20% of people)	**Occasional, some may be serious** (occurs in 4-20% of people)	**Possible, some may be serious** (occurs in 1-3% of people)	**Rare, and serious** (occurs in less than 1% of people)
• In children and adolescents: decreased height • Loss of bone tissue • Mood swings • Skin changes, acne • Swelling of the body, tiredness, bruising • High blood pressure which may cause headaches, dizziness, blurred vision • Pain in belly • Increased appetite and weight gain • Weight gain in the belly, face, back and shoulders	• Cloudiness of the eye, visual disturbances • Glaucoma • Infection • Non-healing wound • Diabetes • Damage to the bone which may cause joint pain and loss of motion • Kidney stones • Heartburn	• Bleeding from sores in the stomach • Broken bones	• Blood clot in vein • Hypersensitivity (allergic) reactions