CEDARS-SINAI MEDICAL CENTER

APPENDIX C

Supplemental Information for Subjects Travelling to Cedars-Sinai From Outside the United States

Title: Treatment of pituitary Cushing disease with a selective CDK inhibitor, R-roscovitine

PARTICIPATING RESEARCHERS:

Shlomo Melmed, MD	Principal Investigator
Ning-Ai Liu, MD	Co-Investigator
Vivien Bonert, MD	Co-Investigator

STUDY CONTACT PHONE NUMBER AT CSMC: 310-423-2830

AFTER HOURS CONTACT (24 HOURS): 310-423-5000

You have indicated an interest in participating in a research study conducted at Cedars-Sinai Medical Center that would require travelling to the research site in Los Angeles, California. Once you arrive at Cedars-Sinai, your participation will follow the details as outlined in the main consent form for the above-referenced study, however, as an international participant, this appendix attempts to address situations that may differ for you. Please read through this appendix carefully and contact one of the investigators above with any questions or concerns.

HOW WILL STUDY PROCEDURES DIFFER FOR INTERNATIONAL PARTICIPANTS?

Screening:

The study team will request access to your medical records maintained by your treating physician, and held by any hospitals where you have had treatments or evaluations for your conditions. Depending on local requirements, you may be asked to sign separate legal releases that would allow these medical records to be shared with the Cedars-Sinai research team. All

information required to determine if you are a good match for this study should be included as part of your existing medical records. There should be no need to conduct additional testing in order to determine your eligibility for this research study.

Washout:

If it is determined that you are a good match for this study, the study requires you to stop taking other drugs for 2 weeks so they may be flushed from your body in order to prevent conflicts with the study drug. For this study, you are required to stop taking metyrapone, ketoconazole, pasireotide, mifepristone, and CYP3A4 inducers or inhibitors for 2 weeks. In addition, you will also be required to discontinue cabergoline for 4 weeks. You will also be required to consult with the researchers before taking any non-study medications including over-the-counter drugs or vitamins. This washout period will be completed before you travel to Cedars-Sinai. It is important that discuss your plan to discontinue these medications with your local physician and advise your local physician of any side effects your may experience as a result of stopping these medications. Possible risks from the washout are discussed in the section "What are the Possible Risks or Discomforts?"

Collection of Pregnancy Outcomes

If you are a female participant and become pregnant during the study, we would like to collect information on the outcome of your pregnancy including spontaneous or voluntary termination, details of the birth, and the presence or absence of any birth defects, abnormalities, or complications. This may require that you sign separate documents to allow Cedars Sinai investigators to have access to your medical records in your home country to review s information about you and your child in the rare case that you become pregnant during your participation in this research study. Becoming pregnant would require your withdrawal from the study, and the study team will work with you to arrange your return to your home country.

If you are a male participant and your female partner becomes pregnant during the study, we will ask your female partner for consent and authorization to collect information on the outcome of her pregnancy and the status of your child, including spontaneous or voluntary termination, details of the birth, and the presence or absence of any birth defects, abnormalities, or complications. This information will be collected from your female partner's medical records with her permission.

Follow-up Visit for Discontinuing Participants

While you are free to discontinue your participation at any time, should you decide to discontinue participation before completing all study visits, 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. Your departure from Cedars-Sinai will be planned in order to accommodate your completion of the Final Study Visit.

WHAT HAPPENS IF MY PARTICIPATION IS STOPPED?

As noted in the main consent form, there are several scenarios which could lead to your discontinuation from participation in the study, including failing to comply with scheduled study visits. Should your participation be discontinued prior to your completion of participation, the study team will work with you to make arrangements to have you return home as soon as possible. The study team will advise you of your departure date and discontinue coverage of any lodging fees beginning on this date.

It is important to note that discontinuation of participation in this study could impact the conditions under which your travel visa was issued. You must work closely with the study team to ensure you continue to meet the restrictions of your visa.

C2. FINANCIAL CONSIDERATIONS

Compensation for Participating

The study will cover the following:

- On study days you will be provided with a single meal voucher.
- Your hotel room will also be paid for by the research team. The research team will only be responsible for the cost of the room in which you will be staying and will not provide compensation should you decide to stay with family or friends.
- You will not be responsible for the cost of traveling to and from Cedars-Sinai Medical Center to attend required study visits.
- As noted in the main consent form, the research requires the conduct of a Visual Field Exam and an MRI of the Pituitary. If this has not been done as part of your standard care, the research study will perform and pay for the costs related to these procedures.
- Cost of the airplane ticket to and from your country of origin to Los Angeles, CA
- Cost of travel to and from the airport to and from your CSMC lodging to attend required study visits

Other costs not covered during your research stay:

- Any additional fees (such as room service, Internet, damage to your room, etc.) incurred at your hotel. incurred at hotel. Daily meals.
- Personal expenses (e.g., groceries, toiletries, clothing, etc)
- Cost of necessary medical care unrelated to study participation (see below for more information)
- Entertainment during your stay (e.g., movie tickets, eating out)
- Transportation costs

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

Who pays for my research related illness or injury?

A research injury or illness is a direct result of the Study Drug, or a procedure performed only as a part of the study and is not part of your standard clinical medical treatment. 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 insurance. Losses such as lost wages will not be paid. If you choose to obtain non-emergency care elsewhere, you or your insurance may be responsible for the costs of that care.

If you become ill or are injured and the cause is not research related, you and/or your insurance will be responsible for the costs of your treatment. This includes incidental injuries and illnesses during your travel or stay in Los Angeles. You will pay for the cost of additional lodging, meals, and other expenses in the event of a non-research related injury or illness that would require you to stay beyond the planned study visit period.