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**Place Patient Identification Sticker Here**

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**Owner Informed Consent**

Study Title: Rapamycin: Evaluation of Effectiveness in Renal Senescence – The REVERSE Study

Principal Investigator: Jessica Quimby, DVM, PhD, DACVIM (Quimby.19@osu.edu; 614-292-3551)

Sponsor: TriviumVet

This form is designed to provide you with information about this study, so you may make an informed decision about your animal’s participation in the project. This study has been reviewed and approved by The OSU Institutional Animal Care and Use Committee.

**Please read the following items.**

**1. What is the purpose of this study?** Evidence exists to suggest that aging of the kidney may contribute to the onset and progression of chronic kidney disease (CKD). Rapamycin is a drug that is a known modulator of the aging process and additionally may decrease the formation of fibrosis (scarring) in the kidney. A feline formulation of the drug is available and the purpose of this study is to assess the potential benefit of the drug in cats with CKD.

**2. Is my cat eligible to participate?** Cats with stable IRIS stage 2 CKD (serum creatinine ≥ 2.0 - 2.8 mg/dL) that are amenable to pill administration and have a body weight > 2.7 kg (6 lbs) are eligible to participate. Exclusion criteria include congenital CKD (dysplasia or polycystic kidney disease), diabetes mellitus, other uncontrolled systemic illnesses, complications of CKD such as kidney infection or ureteral obstruction, moderate to severe anemia (PCV < 25%), decompensed CKD requiring hospitalization and intravenous fluid therapy. Other concurrent therapies such as dietary management, potassium supplementation, anti-hypertensive medications and subcutaneous fluids are acceptable if they were initiated at least 28 days prior to enrollment and are given consistently throughout the study period. Prohibited concurrent therapies include cyclosporine, cisapride, beta-blocking agents, antifungal agents, diltiazem and other medications that could affect rapamycin concentrations.

**3. What procedures/treatments will my cat experience if enrolled in this study?** At the time of screening, your cat will receive a physical examination and comprehensive laboratory screening to confirm stage of CKD and exclude other newly diagnosed conditions (eg. hyperthyroidism, hypertension). At one of the screening visits an abdominal ultrasound and radiographs will also be performed (these procedures typically require light sedation). After confirmation of enrollment, your cat will be randomized to receive Rapamycin or placebo which will be administered orally as a whole tablet (followed with water or food to ensure swallowing) once weekly for 12 weeks. Some cats may require two tablets per dose. You will fill out a quality of life assessment at the beginning of the study and then twice more during the study as well as an owner diary. You will be asked to bring your cat back for three recheck visits (day 14, 42 and 84) for a physical exam, blood and urine collection and blood pressure measurement. A summary of events is presented in the table below.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Procedure | Screening Visit 1  Day -42 to -14 | (Screening Visit 2\*)  (Day -14 to -1) | Enrollment  Day 0 | Day 14  ± 3 | Day 42  ± 7 | Day 84  ± 7 |
| Informed consent | X |  |  |  |  |  |
| Medical history | X | (X) | X | X | X | X |
| Dietary history | X | (X) | X | X | X | X |
| Physical examination | X | (X) | X | X | X | X |
| Quality of life assessment |  |  | X |  | X | X |
| Abdominal radiography | X¥ | (X¥) | X¥ |  |  |  |
| Abdominal ultrasonography | X¥ | (X¥) | X¥ |  |  |  |
| Systolic blood pressure | X | (X) | X | X | X | X |
| Hematology | X | (X) | X | X | X | X |
| Biochemistry | X | (X) | X | X | X | X |
| SDMA | X |  | X | X | X | X |
| Serum cobalamin | X |  |  |  |  |  |
| Total T4 | X | (X) |  |  |  | X |
| FIV/FeLV testing | X |  |  |  |  |  |
| Urinalysis | X | (X) | X |  | X | X |
| FGF-23 |  |  | X |  | X | X |
| Banked plasma and urine |  |  | X |  | X | X |
| Drug dispensing |  |  | X | X | X |  |
| Drug accountability |  |  |  | X | X | X |

\*Screening visit 2 will only be necessary in cats where a correctable condition is identified at the Screening 1 visit that requires a recheck prior to enrollment.

¥ Abdominal radiography and ultrasonography to be completed once; at Screening Visit 1, Screening Visit 2, or prior to enrolment on Day 0.

**4. What are the potential benefits to my cat for participating in this study?** Your cat will receive complimentary assessment and management of disease by a board-certified specialist in feline CKD as well as standard of care laboratory monitoring regardless of study group. Cats randomized to the study drug group will possibility benefit from this therapy.

**5. What are the possible risks to my cat?** Your cat may experience transient stress of being in the hospital and mild discomfort of having blood drawn. If you cat is excessively stressed at any time, we will not continue with drawing the study samples. Gabapentin may be given to alleviate stress before proceeding. If this is not effective, we will discuss with you whether continuing the study is in your cat’s best interest. A blood draw can result in bruising at the site of the blood draw. In rare cases, using a needle to collect urine directly from the bladder may result in hematuria, nausea or very infrequently bladder rupture. Your cat will be observed closely for side effects and appropriate medical care will be provided. Sedation is used for the abdominal ultrasound (this is normal even for cats not in a study) and risks of sedation may include prolonged lethargy or recovery time and highly unlikely, but still possible, decompensation of CKD or unexpected death. The feline formulation of rapamycin used in this study is also being used in a clinical trial of client-owned cats with heart disease at two other universities; no significant drug-related adverse events have been identified to date.

It is possible your cat’s condition may not improve or it may worsen. It is possible your cat may not benefit from this study. Results of this study will not be available immediately. The goal of the study is to acquire information that could be beneficial managing patients with CKD in the future. It is possible that your cat may not benefit directly from this study.

**6. What non-study options are available for my cat?** If your cat does not enroll in the study**,** its CKD will be managed with diet and medical therapy in a similar manner to the way in which it would be if enrolled in the study.

**7.  What are the financial costs and/or benefits associated with enrolling my cat in this study?** There is no cost to you for enrolling your cat in this study. You will receive complimentary physical examination for your cat and diagnostic testing. You will also receive $25 per visit incentive. In the unlikely event that an adverse event that requires treatment occurs as a result of taking part in this study, the cost of treatment will be covered by the study.

**Please initial each statement**

\_\_\_\_I realize that any tests, procedures, or treatments beyond those specifically listed above are my financial responsibility.

\_\_\_\_ I have read the information above and understand the purpose and requirements of the clinical trial entitled "Blinded, randomized placebo-controlled clinical trial of a novel veterinary rapamycin product in cats with chronic kidney disease”

\_\_\_\_I understand that my cat must have a diagnosis of IRIS Stage 2 CKD in order to participate in the study.

\_\_\_\_ After confirmation of enrollment, I understand my cat will need to return for three total visits over the course of the 12 week study period.

\_\_\_\_ Data and fluid samples collected from my cat will become the property of the institution.

\_\_\_\_I give my permission to publish data and images obtained from this study. I understand that all personal identifying information will be removed from scientific publications.

\_\_\_\_If I choose not to participate in this study it will not affect the care of my cat.

\_\_\_\_I may withdraw my cat from this study without penalty. Withdrawal of my cat will not interfere with future care. I understand that investigators may continue to collect information from my cat’s medical record following withdrawal.

\_\_\_\_The study team reserves the right to remove my cat from this study for failure to meet study requirements or if it is in the best interests of my cat.

\_\_\_\_I may discuss this study with others and ask advice from my own veterinarian.

\_\_\_\_ Someone may contact me after my cat has finished this study to collect follow-up treatment and outcome information. This may occur several months to years following completion of the study.

\_\_\_\_I have had time to ask questions regarding this study and feel comfortable moving forward with enrollment in this study based on the information provided.

\_\_\_\_I hereby grant to the College of Veterinary Medicine at The Ohio State University, Columbus, OH the right to publish, broadcast, webcast, or disseminate in any other form or medium any or all of the following:

* Stories, photographs, video, audio, and other images or likenesses of my animal for use in news stories, publications, promotional materials, including advertisements, web features and/or any other official purposes.
* I understand that I will not receive financial compensation for this use.
* All photographs, video, audio, images, likenesses, stories, and other materials will remain the property of Ohio State.

For additional questions or concerns about the study, please contact *Dr. Jessica Quimby* at Quimby.19@osu.edu. Or if you would like to discuss any concerns with an individual not directly related with the study, please contact Ms. Lora Montgomery, Assistant Director, Customer Service at 614-292-5772 (Montgomery.1012@osu.edu)

As a result of discussion with \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, and after reading the above, I voluntarily consent for my [species] to participate in this study and will follow the instructions of the study team, as it pertains to therapy and follow-up procedures. I certify that I am the legal owner/guardian of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

Signed \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Owner or authorized agent of the owner

Witnessed By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_