

**Supplemental Table 1. Mean arterial blood pressure (MAP) in low-dose, standard-dose and standard care at baseline, 3, 6, 9, and 12 months for the 26 patients completing the study\***

|                         | Low-dose<br>Rapamycin<br>(n=9) | Standard-dose<br>Rapamycin<br>(n=8) | Standard Care<br>(n=9) |
|-------------------------|--------------------------------|-------------------------------------|------------------------|
| Baseline MAP†<br>(n=26) | 93.8 ± 7.6<br>(n=9)            | 100.0 ± 9.1<br>(n=8)                | 90.1 ± 7.5<br>(n=9)    |
| 3-month MAP†<br>(n=26)  | 92.2 ± 9.3<br>(n=9)            | 95.9 ± 12.1<br>(n=8)                | 88.7 ± 10.7<br>(n=9)   |
| 6-month MAP†<br>(n=26)  | 91.1 ± 8.1<br>(n=9)            | 99.0 ± 6.6<br>(n=8)                 | 91.9 ± 7.6<br>(n=9)    |
| 9-month MAP†<br>(n=26)  | 87.6 ± 7.9<br>(n=9)            | 95.9 ± 4.2<br>(n=8)                 | 92.3 ± 8.8<br>(n=9)    |
| 12-month MAP†<br>(n=26) | 92.5 ± 12.1<br>(n=9)           | 102.7 ± 5.4<br>(n=8)                | 93.8 ± 10.1<br>(n=9)   |

\*Overall MAP levels were higher in the standard-dose rapamycin group as compared to the low-dose rapamycin group ( $P=0.03$ ) and the standard care group ( $P=0.01$ ), but there was no significant changes in MAP levels over time by group ( $P=0.34$ ) or time overall ( $P=0.26$ ).

†mmHg, ± SD

**Supplemental Table 2. Rapamycin trough blood levels during the 12 month course of low-dose or standard-dose rapamycin\***

|          | Low-Dose         | Standard-Dose    |
|----------|------------------|------------------|
| Week 1   | 2.90 ± 1.20† (9) | 4.34 ± 2.58† (8) |
| Week 2   | 2.76 ± 1.32 (9)  | 4.71 ± 2.53 (8)  |
| Week 4   | 2.62 ± 1.18 (9)  | 3.93 ± 2.27 (8)  |
| Week 6   | 2.55 ± 0.72 (8)  | 4.69 ± 1.85 (8)  |
|          |                  |                  |
| Month 3  | 2.73 ± 4.61 (8)  | 4.61 ± 1.72 (7)  |
| Month 6  | 2.55 ± 0.76 (8)  | 4.23 ± 1.65 (6)  |
| Month 9  | 2.40 ± 0.64 (7)  | 5.77 ± 1.06 (6)  |
| Month 12 | 2.68 ± 0.26 (5)  | 4.60 ± 1.02 (4)  |

\*Based on the results of the mixed model, low-dose patients had significantly lower trough levels of rapamycin than standard-dose patients over the course of the study ( $P<0.001$ ).

† ng/mL, mean ± SD

() *n*

**Supplemental Table 3. Total liver volume (TLV) and changes during 12 months of rapamycin treatment or standard care\***

|                                        | Low-dose<br>Rapamycin<br>(n=10)          | Standard-dose<br>Rapamycin<br>(n=10)     | Standard Care<br>(n=10)                     | P Value† |
|----------------------------------------|------------------------------------------|------------------------------------------|---------------------------------------------|----------|
| Baseline TLV‡<br>(n=30)                | 1,711.2 ± 315.3<br>(n=10)                | 2,136.8 ± 678.0<br>(n=10)                | 2,128.9 ± 956.3<br>(n=10)                   | 0.24     |
| 6-month TLV‡<br>TLV change‡<br>(n=29)  | 1,787.2 ± 303.6<br>51.7 ± 92.9<br>(n=10) | 1,913.7 ± 477.0<br>-68.1 ± 53.6<br>(n=9) | 2,195.9 ± 1,024.8<br>67.0 ± 202.3<br>(n=10) | 0.12     |
| 12-month TLV‡<br>TLV change‡<br>(n=26) | 1,825.6 ± 380.4<br>90.0 ± 149.7<br>(n=9) | 1,811.9 ± 313.9<br>-51.1 ± 89.5<br>(n=8) | 2,314.7 ± 1,268.1<br>177.0 ± 336.0<br>(n=9) | 0.18     |

\* Mixed model results indicated no significant differences in overall group levels ( $P=0.46$ ), changes in group over time ( $P=0.69$ ) or overall changes over time ( $P=0.70$ )

†P value based on ANOVA

‡cc, mean ± SD

**Supplemental Table 4. Changes in hemoglobin, platelet count, fasting LDL cholesterol and triglycerides, and serum magnesium at baseline and after 12 months of rapamycin or standard care**

|                                                       | Low-dose Rapamycin LD (n=10) | Standard-dose Rapamycin STD (n=10) | Standard Care SC (n=10)      | P Value*      |
|-------------------------------------------------------|------------------------------|------------------------------------|------------------------------|---------------|
| Hemoglobin (g/dL)†‡<br>12 month change (g/dL)‡        | 14.2 ± 1.5<br>-0.6 ± 1.1     | 14.4 ± 1.3<br>-0.1 ± 1.0           | 14.6 ± 0.7<br>-0.5 ± 0.7     | 0.78<br>0.60  |
| Platelet count (k/μL)†‡<br>12 month change (k/μL)‡    | 226.9 ± 32.3<br>12.3 ± 29.3  | 255.0 ± 26.9<br>17.6 ± 28.6        | 231.1 ± 37.4<br>-19.4 ± 27.4 | 0.01<br>0.02§ |
| LDL cholesterol (mg/dL)†‡<br>12 month change (mg/dL)‡ | 99.7 ± 36.2<br>12.0 ± 38.7   | 111.4 ± 27.7<br>1.2 ± 23.0         | 112.9 ± 19.7<br>-15.4 ± 21.3 | 0.49<br>0.13  |
| Triglycerides (mg/dL)†‡<br>12 month change (mg/dL)‡   | 105.5 ± 57.2<br>-2.0 ± 43.5  | 141.4 ± 77.6<br>3.3 ± 54.9         | 145.2 ± 79.0<br>-22.7 ± 90.6 | 0.22<br>0.32  |
| Serum magnesium (mg/dL)†‡<br>12 month change (mg/dL)‡ | 2.2 ± 0.3<br>-0.1 ± 0.3      | 2.1 ± 0.3<br>-0.1 ± 0.2            | 2.1 ± 0.2<br>0.0 ± 0.2       | 0.70<br>0.50  |

\*P value based on ANOVA

†baseline

‡mean, ± SD

§P value for adjusted (Tukey) pairwise comparisons: LD vs SC  $P=0.05$ , STD vs SC  $P=0.02$ , LD vs STD  $P=0.91$ , LD+STD vs SC  $P=0.005$

**Supplemental Table 5. Additional medications during 12 months of rapamycin or standard care.**

|                                                | Low-dose Rapamycin LD ( <i>n</i> =10) | Standard-dose Rapamycin STD ( <i>n</i> =10) | Standard Care SC ( <i>n</i> =10) | <i>P</i> Value* |
|------------------------------------------------|---------------------------------------|---------------------------------------------|----------------------------------|-----------------|
| ACEI†                                          | 4                                     | 4                                           | 6                                | 0.72            |
| ARB†                                           | 7                                     | 10                                          | 6                                | 0.15            |
| ACEI and/or ARB                                | 9                                     | 10                                          | 9                                | >0.99           |
| ACEI and ARB                                   | 2                                     | 4                                           | 3                                | 0.88            |
| Statin                                         | 7                                     | 8                                           | 7                                | >0.99           |
| Triglyceride lowering medication‡              | 1                                     | 4                                           | 2                                | 0.43            |
| Statin and/or Triglyceride lowering medication | 8                                     | 8                                           | 7                                | >0.99           |
| Statin and Triglyceride lowering medication    | 0                                     | 4                                           | 2                                | 0.12            |
| Diuretic§                                      | 0                                     | 6                                           | 2                                | 0.01**          |

\**P* value based on Chi-square test

† angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB)

‡ fibric acid derivative or omega-3

§ see text for explanation of diuretic use

\*\*adjusted (Bonferroni) pairwise comparisons: LD vs SC *P*=0.47, STD vs SC *P*=0.17, LD vs STD *P*=0.01, LD+STD vs SC *P*=0.68

## Supplemental Figure 1

Title:

Total Kidney Volume (TKV) with absolute change during 12 months of rapamycin treatment or standard care

Caption:

*P* value based on ANOVA: baseline *P*=0.54; change at 12 months *P*=0.33. Mean ( $\pm$ SD), median, 25<sup>th</sup>, and 75<sup>th</sup> percentile change in TKV: (LD) 197.7 ( $\pm$ 201.2), 143.0, 126.0, and 201.0 cc, respectively; (STD) 82.9 ( $\pm$ 111.3), 51.5, 30.5, 81.5 cc, respectively; and (SC) 152.7 ( $\pm$ 129.4), 129.0, 52.0, and 189.0 cc, respectively.

