

**Table S1.** Intra-group and against control comparisons of clinically relevant metabolic markers concentration among groups and doses during the five-week dose-escalation period in lean participants.

|                      | Daily dose | Variable       |                |                   |                          |                  |                   |
|----------------------|------------|----------------|----------------|-------------------|--------------------------|------------------|-------------------|
|                      |            | GLU<br>(mg/dL) | TRG<br>(mg/dL) | CHOL-T<br>(mg/dL) | HDL-C<br>(mg/dL)         | LDL-C<br>(mg/dL) | VLDL-C<br>(mg/dL) |
| AGAVINS              | 0 g        | 83.8 ± 2.5     | 157.1 ± 24.9   | 205.9 ± 14.6      | 50.66 ± 4.1              | 126.5 ± 13.7     | 31.47 ± 5         |
|                      | 2.5 g      | 82.13 ± 2.4    | 130.1 ± 20.1   | 197.5 ± 15.3      | 50.41 ± 4.8              | 124.1 ± 14.4     | 26 ± 4            |
|                      | 5 g        | 82.88 ± 2.3    | 130.1 ± 19.3   | 203.4 ± 11.6      | 51.86 ± 5.1              | 129.5 ± 11.2     | 26.10 ± 3.9       |
|                      | 7 g        | 84.25 ± 3.6    | 126.1 ± 15.1   | 204.5 ± 15.4      | 53.86 ± 5.3 <sup>b</sup> | 130.1 ± 15       | 25.20 ± 3         |
|                      | 10 g       | 80.89 ± 4.1    | 147.9 ± 21.4   | 200 ± 13          | 49.79 ± 4.6 <sup>b</sup> | 123.4 ± 13.5     | 29.56 ± 4.2       |
|                      | 12 g       | 84.33 ± 2.5    | 113.9 ± 14     | 202.4 ± 13.5      | 53.14 ± 3.9              | 130.8 ± 11.5     | 22.78 ± 2.8       |
| PLACEBO              | 0 g        | 82 ± 3.2       | 105.8 ± 12.4   | 196.2 ± 12.4      | 51.84 ± 3.9              | 123.2 ± 9.3      | 21.17 ± 2.4       |
|                      | 2.5 g      | 83.28 ± 3.1    | 99.57 ± 18.4   | 195.8 ± 13.7      | 54.55 ± 4.8              | 121.3 ± 10.9     | 20 ± 3.6          |
|                      | 5 g        | 79.66 ± 3.6    | 93 ± 17.8      | 197.8 ± 18.8      | 53 ± 4.4                 | 126.1 ± 14.5     | 18.66 ± 3.6       |
|                      | 7 g        | 84.28 ± 1.9    | 101.2 ± 16.7   | 195.7 ± 19.1      | 55.57 ± 5.5              | 119.8 ± 14.6     | 20.31 ± 3.3       |
|                      | 10 g       | 86.57 ± 1.4    | 95.28 ± 21     | 201 ± 18.1        | 53.32 ± 5.2              | 128.8 ± 13.8     | 30.42 ± 10.6      |
|                      | 12 g       | 81.28 ± 5.8    | 103.8 ± 25.4   | 196.2 ± 13.2      | 51.88 ± 2.6              | 123.6 ± 10.7     | 20.77 ± 5         |
| P value <sup>a</sup> |            | 0.567          | 0.191          | 0.402             | 0.225                    | 0.336            | 0.193             |

Abbreviations: CHOL-T, total cholesterol; GLU, fasting glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TRG, triglycerides; VLDL-C, very-low-density lipoprotein density. Data presented as mean ± SEM. <sup>a</sup>Obtained from a mixed-effects analysis with the Geisser-Greenhouse correction for agavins doses treatment. <sup>b</sup>Significant difference ( $P < .05$ ) between 7 g/day and 10 g/day of agavins, Tukey's multiple comparisons test.

**Table S2.** Intra-group and against control comparisons of clinically relevant metabolic markers concentration among groups and doses during the five-week dose-escalation period in obese participants.

|                      | Daily dose | Variable       |                           |                          |                  |                  |                          |
|----------------------|------------|----------------|---------------------------|--------------------------|------------------|------------------|--------------------------|
|                      |            | GLU<br>(mg/dL) | TRG<br>(mg/dL)            | CHOL-T<br>(mg/dL)        | HDL-C<br>(mg/dL) | LDL-C<br>(mg/dL) | VLDL-C<br>(mg/dL)        |
| AGAVINS              | 0 g        | 83.64 ± 4      | 164.5 ± 30.5              | 176.6 ± 12.1             | 41.45 ± 3.1      | 102.3 ± 8.1      | 32.93 ± 6.1              |
|                      | 2.5 g      | 84.82 ± 2.6    | 176.3 ± 28.4              | 177.4 ± 14.3             | 38.93 ± 2.7      | 103.1 ± 10.7     | 35.36 ± 5.6              |
|                      | 5 g        | 88.70 ± 3      | 219.7 ± 31.1 <sup>b</sup> | 181.9 ± 12.8             | 37.09 ± 2.4      | 100.8 ± 7.6      | 43.94 ± 6.2 <sup>d</sup> |
|                      | 7 g        | 80.91 ± 1.9    | 238 ± 35.9                | 182.8 ± 12.3             | 39.85 ± 2.5      | 95.34 ± 8.6      | 47.64 ± 7.1              |
|                      | 10 g       | 81.13 ± 3.1    | 145 ± 22.2                | 161.4 ± 6.6 <sup>c</sup> | 40.91 ± 2.6      | 91.55 ± 6.3      | 29.13 ± 4.4              |
|                      | 12 g       | 84.45 ± 3.1    | 195.7 ± 31.8              | 180.9 ± 11.9             | 40.71 ± 2.6      | 101.1 ± 8.4      | 39.15 ± 6.3              |
| PLACEBO              | 0 g        | 85.27 ± 3.1    | 151.9 ± 20.1              | 173.7 ± 7.8              | 41.29 ± 3.1      | 102 ± 5.5        | 30.36 ± 4                |
|                      | 2.5 g      | 83 ± 2.5       | 136.1 ± 14                | 177.3 ± 7.3              | 44.25 ± 2.6      | 105.9 ± 6.6      | 27.04 ± 2.8              |
|                      | 5 g        | 85.18 ± 2.7    | 137.7 ± 11.8 <sup>b</sup> | 171.4 ± 6.3              | 43.35 ± 2.9      | 100.4 ± 5.7      | 27.54 ± 2.4 <sup>d</sup> |
|                      | 7 g        | 88.8 ± 4.6     | 177.6 ± 20                | 184.3 ± 5.2              | 43.85 ± 2        | 104.9 ± 5.6      | 35.52 ± 4                |
|                      | 10 g       | 85.09 ± 2.6    | 165.2 ± 23.3              | 183.1 ± 4.7 <sup>c</sup> | 45.67 ± 3.1      | 103.6 ± 3.4      | 33.09 ± 4.6              |
|                      | 12 g       | 83.45 ± 2.5    | 186.9 ± 22.7              | 178.8 ± 4.8              | 42.01 ± 2.8      | 99.41 ± 4.3      | 37.38 ± 4.5              |
| P value <sup>a</sup> |            | 0.448          | 0.098                     | 0.881                    | 0.557            | 0.680            | 0.099                    |

Abbreviations: CHOL-T, total cholesterol; GLU, fasting glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TRG, triglycerides; VLDL-C, very-low-density lipoprotein density. Data presented as mean ± SEM. <sup>a</sup>Obtained from a mixed-effects analysis with the Geisser-Greenhouse correction for agavins doses treatment. <sup>b,c,d</sup>Significant differences between agavins and placebo groups ( $P < .05$ ) after the same dose, unpaired t test with Welch's correction.

**Table S3.** Body composition analysis during the five-week dose-escalation period in lean participants.

|                             | Daily dose | Variable    |             |             |             |             |             |              |
|-----------------------------|------------|-------------|-------------|-------------|-------------|-------------|-------------|--------------|
|                             |            | BW (Kg)     | RFM (Kg)    | AFM (Kg)    | FFM (Kg)    | SMM (Kg)    | TBW (L)     | EW (L)       |
| AGAVINS                     | 0 g        | 60.58 ± 1.5 | 28.89 ± 2.2 | 17.42 ± 1.2 | 43.16 ± 1.9 | 19.46 ± 1.2 | 31.6 ± 1.3  | 13.03 ± 0.33 |
|                             | 2.5 g      | 60.66 ± 1.6 | 29.51 ± 2.5 | 17.83 ± 1.4 | 42.82 ± 2   | 19.29 ± 1.2 | 31.34 ± 1.3 | 12.93 ± 0.31 |
|                             | 5 g        | 60.97 ± 1.9 | 29.29 ± 2.7 | 17.75 ± 1.5 | 43.22 ± 2.4 | 19.37 ± 1.4 | 31.66 ± 1.5 | 13.2 ± 0.41  |
|                             | 7 g        | 60.72 ± 1.7 | 29.99 ± 2.3 | 18.11 ± 1.3 | 42.61 ± 2.1 | 19.37 ± 1.2 | 31.28 ± 1.3 | 12.87 ± 0.33 |
|                             | 10 g       | 60.96 ± 1.6 | 29.94 ± 2.4 | 18.19 ± 1.4 | 42.76 ± 2   | 19.09 ± 1.2 | 31.27 ± 1.3 | 13.07 ± 0.31 |
|                             | 12 g       | 60.56 ± 1.6 | 29.57 ± 2.4 | 17.87 ± 1.4 | 42.69 ± 1.9 | 19.43 ± 1.1 | 31.3 ± 1.2  | 12.84 ± 0.34 |
| PLACEBO                     | 0 g        | 62.57 ± 3.8 | 24.38 ± 2.1 | 15.39 ± 1.7 | 47.15 ± 3   | 21.32 ± 1.9 | 34.56 ± 2.1 | 14.34 ± 0.92 |
|                             | 2.5 g      | 62.21 ± 3.9 | 23.97 ± 2.0 | 15.08 ± 1.6 | 47.26 ± 3.1 | 21.6 ± 2    | 34.78 ± 2.3 | 14.32 ± 0.92 |
|                             | 5 g        | 63.01 ± 4.5 | 23.24 ± 1.5 | 14.89 ± 1.9 | 48.29 ± 3.3 | 22.02 ± 2   | 35.32 ± 2.3 | 14.54 ± 1    |
|                             | 7 g        | 62.61 ± 3.9 | 24.06 ± 2.2 | 15.16 ± 1.5 | 47.48 ± 3   | 21.23 ± 1.9 | 34.73 ± 2.2 | 14.56 ± 0.93 |
|                             | 10 g       | 62.19 ± 3.9 | 24.38 ± 2.2 | 15.36 ± 1.6 | 47.15 ± 2.9 | 20.97 ± 1.9 | 34.24 ± 2.2 | 14.32 ± 0.89 |
|                             | 12 g       | 61.74 ± 4.3 | 23.7 ± 1.9  | 14.78 ± 1.5 | 48.36 ± 3.2 | 21.11 ± 1.9 | 34.34 ± 2.3 | 14.29 ± 1    |
| <i>P</i> value <sup>a</sup> |            | 0.123       | 0.114       | 0.153       | 0.265       | 0.156       | 0.197       | 0.123        |

Abbreviations: BW, body weight; RFM, relative fat mass; AFM, absolute fat mass; FFM, fat-free mass; SMM, skeletal muscle mass; TBW, total body water; EW, extracellular water. <sup>a</sup>Obtained from a mixed-effects analysis with the Geisser-Greenhouse correction for agavins dose treatment. No significant differences ( $P < .05$ ) for intra-group comparisons in agavins group by Holm-Šidák's multiple comparisons test, nor for comparisons against control for each dose by an unpaired t test with Welch's correction.

**Table S4.** Body composition analysis during the five-week dose-escalation period in obese participants.

|                             | Daily dose | Variable                 |             |             |             |             |             |              |
|-----------------------------|------------|--------------------------|-------------|-------------|-------------|-------------|-------------|--------------|
|                             |            | BW (Kg)                  | RFM (Kg)    | AFM (Kg)    | FFM (Kg)    | SMM (Kg)    | TBW (L)     | EW (L)       |
| AGAVINS                     | 0 g        | 88.43 ± 3.5 <sup>b</sup> | 43.13 ± 1.9 | 38.16 ± 2.3 | 50.27 ± 2.7 | 23.27 ± 1.6 | 37.27 ± 2   | 16.41 ± 0.68 |
|                             | 2.5 g      | 88.23 ± 3.7              | 43.66 ± 1.8 | 38.58 ± 2.4 | 49.65 ± 2.6 | 23.24 ± 1.5 | 36.83 ± 1.9 | 16 ± 0.69    |
|                             | 5 g        | 89.72 ± 3.6              | 43.35 ± 2   | 38.89 ± 2.4 | 50.82 ± 2.8 | 23.74 ± 1.6 | 37.68 ± 2   | 16.44 ± 0.74 |
|                             | 7 g        | 88.21 ± 3.5              | 43.36 ± 1.9 | 38.28 ± 2.4 | 49.93 ± 2.7 | 23.15 ± 1.5 | 36.99 ± 1.9 | 16.25 ± 0.72 |
|                             | 10 g       | 85.07 ± 4 <sup>b</sup>   | 42.79 ± 2.4 | 36.61 ± 3   | 48.46 ± 2.7 | 22.55 ± 1.5 | 35.92 ± 1.9 | 15.62 ± 0.72 |
|                             | 12 g       | 87.44 ± 3.9              | 42.46 ± 2.2 | 37.28 ± 2.7 | 50.16 ± 2.8 | 23.52 ± 1.6 | 37.2 ± 2    | 16.11 ± 0.77 |
| PLACEBO                     | 0 g        | 85.46 ± 4                | 39.59 ± 2.2 | 33.85 ± 2.7 | 51.61 ± 2.9 | 23.74 ± 1.8 | 38.16 ± 2.2 | 16.69 ± 0.8  |
|                             | 2.5 g      | 84.48 ± 4.1              | 39.83 ± 2.4 | 33.66 ± 2.8 | 50.82 ± 3.1 | 23.3 ± 1.8  | 37.61 ± 2.3 | 16.44 ± 0.82 |
|                             | 5 g        | 85.25 ± 3.8              | 39.36 ± 2.4 | 33.51 ± 2.7 | 51.74 ± 3.1 | 23.66 ± 1.8 | 38.19 ± 2.3 | 16.81 ± 0.83 |
|                             | 7 g        | 84.27 ± 3.9              | 38.76 ± 2.6 | 32.56 ± 2.7 | 51.71 ± 3.3 | 23.63 ± 2   | 38.07 ± 2.4 | 16.62 ± 0.8  |
|                             | 10 g       | 85.19 ± 3.7              | 39.34 ± 2.5 | 33.45 ± 2.6 | 51.74 ± 3.1 | 23.77 ± 1.8 | 38.23 ± 2.3 | 16.76 ± 0.79 |
|                             | 12 g       | 85.24 ± 3.7              | 39.27 ± 2.5 | 33.44 ± 2.7 | 51.8 ± 3.1  | 23.7 ± 1.8  | 38.24 ± 2.3 | 16.88 ± 0.78 |
| <i>P</i> value <sup>a</sup> |            |                          |             |             |             |             |             |              |

Abbreviations: BW, body weight; RFM, relative fat mass; AFM, absolute fat mass; FFM, fat-free mass; SMM, skeletal muscle mass; TBW, total body water; EW, extracellular water. <sup>a</sup>Obtained from a mixed-effects analysis with the Geisser-Greenhouse correction for agavins dose treatment. <sup>b</sup>Significant difference ( $P < .05$ ) between 0 and 10 g/day of agavins, Holm-Šidák's multiple comparisons test.