## SUPPLEMENTAL MATERIAL

**Supplementary Table 1.**
**Baseline characteristics and echocardiography results in ZSF1 rats at 8, 14, 20 wks of age**

| Parameter | Lean ZSF1 | | | Obese ZSF1 | | |
|---|---|---|---|---|---|---|
| | 8 wks | 14 wks | 20 wks | 8 wks | 14 wks | 20 wks |
| MABP (mmHg) | - | 143 ± 20 | 148 ± 6 | - | 143 ± 6 | 154 ± 8 |
| Body Weight (g) | - | 378 ± 17 | 472 ± 48 | - | 516 ± 34*** | 635 ± 62*** |
| Glucose (mg/dL) | - | 237 ± 36 | 214 ± 35 | - | 324 ± 53* | 303 ± 70** |
| SubQ Fat (g) | - | 10.0 ± 0.8 | 13.6 ± 3.8 | - | 52.3 ± 4.3*** | 62 ± 13*** |
| RetroP Fat (g) | - | 4.8 ± 0.3 | 6.3 ± 1.3 | - | 16.2 ± 1.7*** | 33.2 ± 4.8*** |
| HW (mg) | - | 1243 ± 25 | 1455 ± 112 | - | 1456 ± 101 | 1722 ± 190*** |
| RV Weight (mg) | - | 208 ± 87 | 278 ± 51 | - | 278 ± 43 | 377 ± 70** |
| LV Weight (mg) | - | 1017 ± 25 | 1099 ± 134 | - | 1294 ± 103* | 1287 ± 160* |
| HW/TL | - | 31.5 ± 0.6 | 35.0 ± 2.6 | - | 38.9 ± 2.2* | 42.8 ± 3.9*** |
| RV/TL | - | 5.2 ± 2.2 | 6.3 ± 1.3 | - | 7.4 ± 1.2* | 9.2 ± 1.4*** |
| LV/TL | - | 25.7 ± 0.8 | 25.9 ± 3.2 | - | 31.2 ± 2.9 | 31.8 ± 4.2** |
| HR (bpm) | 388 ± 16 | 395 ± 20 | 394 ± 16 | 365 ± 33 | 337 ± 36*** | 303 ± 17*** |
| LV Mass (mg) | 803 ± 71 | 1160 ± 67 | 1206 ± 106 | 869 ± 31 | 1607 ± 178*** | 1773 ± 123*** |
| LVAW; d (mm) | 1.45 ± 0.2 | 1.71 ± 0.3 | 1.82 ± 0.3 | 1.68 ± 0.3 | 2.17 ± 0.2** | 2.42 ± 0.3*** |
| LVAW; s (mm) | 3.22 ± 0.3 | 3.18 ± 0.3 | 3.59 ± 0.3 | 3.12 ± 0.2 | 3.45 ± 0.2 | 4.08 ± 0.3** |
| LVID; d (mm) | 6.43 ± 0.5 | 7.39 ± 0.3 | 7.48 ± 0.3 | 6.17 ± 0.2 | 7.74 ± 0.2 | 7.75 ± 0.3 |
| LVID; s (mm) | 2.30 ± 0.4 | 3.17 ± 0.3 | 3.14 ± 0.3 | 2.67 ± 0.3 | 3.33 ± 0.2 | 3.2 ± 0.3 |
| LVPW; d (mm) | 2.21 ± 0.2 | 2.31 ± 0.3 | 2.30 ± 0.3 | 2.30 ± 0.20 | 2.62 ± 0.2** | 2.89 ± 0.3*** |
| LVPW; s (mm) | 3.48 ± 0.3 | 3.81 ± 0.3 | 3.84 ± 0.3 | 3.48 ± 0.40 | 4.38 ± 0.2** | 4.39 ± 0.3*** |
| EF (%) | 92 ± 2 | 89 ± 3 | 88 ± 3 | 89 ± 2 | 87 ± 2 | 87 ± 3 |
| FS (%) | 64.3 ± 1.0 | 60.8 ± 4.8 | 58.7 ± 4.5 | 60.4 ± 2.4 | 57.8 ± 2.6 | 58.8 ± 2.5 |
| SV (μL) | 181 ± 38 | 249 ± 8 | 255 ± 19 | 153 ± 16 | 264 ± 17 | 266 ± 28 |
| CO (mL/min) | 70 ± 14 | 99 ± 6 | 100 ± 10 | 56 ± 5 | 89 ± 10 | 81 ± 8*** |

| | | | | | | |
|---|---|---|---|---|---|---|
| E/A Ratio | 1.83 ± 0.3 | 1.84 ± 0.3 | 1.90 ± 0.3 | 1.72 ± 0.2 | 1.71 ± 0.2 | 1.39 ± 0.3*** |
| DT (ms) | 14.0 ± 1.0 | 14.6 ± 1.4 | 12.7 ± 1.6 | 15 ± 1.4 | 16.3 ± 1.9 | 22.5 ± 3.4*** |

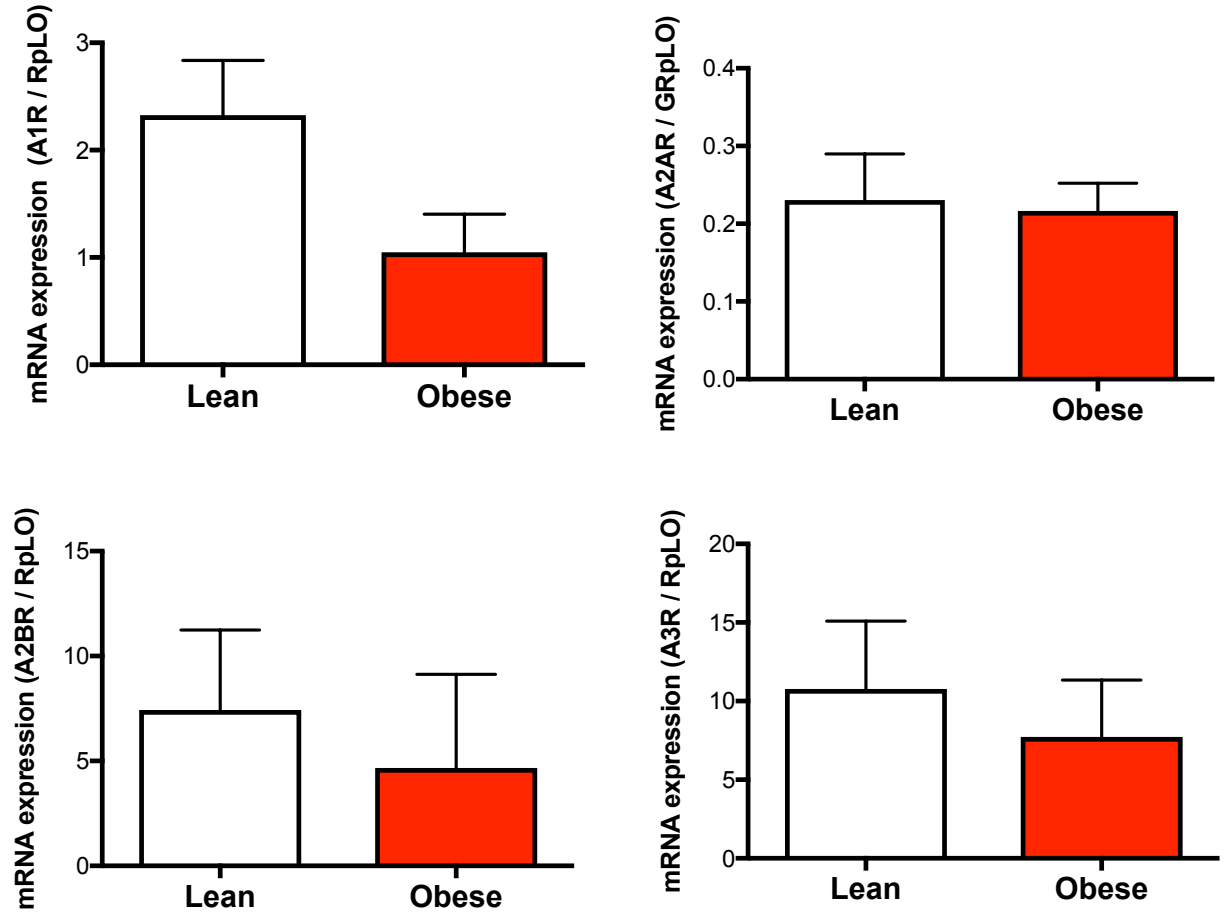
Data are shown as Mean ± SD. Data was analyzed by two-way ANOVA. * indicates $p < 0.05$, ** indicates $p < 0.01$, *** indicates $p < 0.001$ compared between age matched lean and obese ZSF1 groups composed of at least 6 animals per groups. MABP, mean arterial blood pressure; HR, heart rate; BW, body weight; SubQ Fat, subcutaneous fat; RetroP Fat, retroperitoneal fat; HW, heart weight; RV, right ventricle; LV, left ventricle; TL, tibia length; LV, left ventricle; LVAW, left ventricle anterior wall thickness at end diastole (d) or end systole (s); LVID, left ventricular internal diameter at end diastole (d) or end systole (s); LVPW, left ventricle posterior wall thickness at end diastole (d) or end systole (s); EF, ejection fraction; FS, fraction shortening; SV, stroke volume; CO, cardiac output; E/A ratio, peak velocity of early/late mitral inflow ratio; DT, deceleration time; - indicates no data was collected.

**Supplementary Table 2.**
**Echocardiography results and characteristics of ZSF1 rats in ABT-702 treatment study**

| | Lean ZSF1: Vehicle to Vehicle | | | Lean ZSF1: ABT-702 to Vehicle | | |
|---|---|---|---|---|---|---|
| **Parameter** | **16 wks** | **24 wks** | **32 wks** | **16 wks** | **24 wks** | **32 wks** |
| HR (bpm) | 416 ± 14 | 409 ± 2 | 418 ± 4 | 397 ± 13 | 394 ± 12 | 411 ± 8 |
| LV Mass (mg) | 1162 ± 110 | 1223 ± 68 | 1170 ± 82 | 1177 ± 37 | 1268 ± 49 | 1232 ± 140 |
| LVAW; d (mm) | 1.77 ±0.2 | 1.87 ± 0.3 | 1.90 ± 0.3 | 1.90 ± 0.3 | 1.87 ± 0.2 | 1.82 ± 0.3 |
| LVAW; s (mm) | 3.47 ± 0.03 | 3.80 ± 0.3* | 3.89 ± 0.3* | 3.55 ± 0.3 | 3.75 ± 0.3 | 3.88 ± 0.3 |
| LVID; d (mm) | 7.55 ± 0.3 | 7.68 ±0.3 | 7.58 ± 0.4 | 7.50 ± 0.4 | 7.94 ± 0.3 | 8.06 ± 0.2 |
| LVID; s (mm) | 3.1 ± 0.2 | 3.03 ± 0.3 | 2.91 ± 0.3 | 3.0 ± 0.3 | 3.19 ± 0.2 | 3.29 ± 0.2 |
| LVPW; d (mm) | 2.12 ± 0.2 | 2.18 ± 0.3 | 2.08 ± 0.2 | 2.12 ± 0.2 | 2.12 ± 0.2 | 2.02 ± 0.2 |
| LVPW; s (mm) | 4.0 ± 0.2 | 3.98 ± 0.3 | 3.79 ± 0.3 | 3.99 ± 0.3 | 4.00 ± 0.2 | 3.84 ± 0.31 |
| EF (%) | 88 ± 2 | 88 ± 2 | 89 ± 2 | 88 ± 2 | 88 ± 2 | 87 ± 2 |
| FS (%) | 59.2 ± 1.4 | 59.1 ± 1.0 | 61.1 ± 2.3 | 59.1 ± 2.8 | 59.3 ± 3.2 | 58.3 ± 2.8 |
| SV (µL) | 268 ± 38 | 268 ± 22 | 274 ± 26 | 245 ± 44 | 294 ± 10 | 297 ± 30 |
| CO (mL/min) | 112 ± 16 | 109 ± 10 | 115 ± 12 | 97 ± 16 | 116 ± 6 | 122 ± 14* |
| E/A Ratio | 1.98 ± 0.3 | 1.97 ± 0.3 | 1.96 ± 0.3 | 1.92 ± 0.3 | 1.97 ± 0.3 | 1.97 ± 0.3 |
| DT (msec) | 11.0 ± 0.2 | 11.8 ± 0.4 | 11.6 ± 0.4 | 11.3 ± 0.2 | 12.5 ± 1.0 | 12.3 ± 0.6 |
| BP (mmHg) | - | - | 134 ± 8 | - | - | 131 ± 22 |
| Body Weight (g) | - | - | 526 ± 20 | - | - | 517 ± 62 |
| SubQ Fat (g) | - | - | 18 ± 4 | - | - | 20 ± 6 |
| RetroP Fat (g) | - | - | 6 ± 2 | - | - | 7 ± 2 |
| H Weight (mg) | - | - | 1547 ± 102 | - | - | 1535 ± 148 |
| HW/TL | - | - | 35.2 ± 2.0 | - | - | 35.3 ± 4.0 |
| Lung Weight/TL | - | - | 36.1 ± 2.8 | - | - | 38.2 ± 3.6 |

| | Obese ZSF1: Vehicle to ABT-702 | | | Obese ZSF1: ABT-702 to Vehicle | | |
|---|---|---|---|---|---|---|
| **Parameter** | **16 wks** | **24 wks** | **32 wks** | **16 wks** | **24 wks** | **32 wks** |
| HR (bpm) | 347 ± 8[#] | 352 ± 8[#] | 323 ± 6[#] | 358 ± 28[#] | 357 ± 18[#] | 352 ± 16[#] |
| LV Mass (mg) | 1594 ± 54[#] | 1842±174 [*#] | 1883 ± 186[*#] | 1519 ± 124[#] | 1598 ± 52[#] | 1864 ± 162[*$#] |
| LVAW; d (mm) | 2.20 ± 0.2[#] | 2.27 ± 0.2[#] | 2.51 ± 0.2[*$#] | 2.17 ± 0.2[#] | 2.17 ± 0.2[#] | 2.51 ± 0.2[*$#] |
| LVAW; s (mm) | 3.68 ± 0.2 | 4.15 ± 0.2[*#] | 4.30 ± 0.2[*$#] | 3.74 ± 0.3 | 4.05 ± 0.2[#] | 4.34 ± 0.2[*$#] |
| LVID; d (mm) | 7.54 ± 0.5 | 8.00 ± 0.2 | 7.66 ± 0.5 | 7.75 ± 0.5 | 8.09 ± 0.2 | 7.65 ± 0.5 |
| LVID; s (mm) | 3.06 ± 0.2 | 3.15 ± 0.2 | 3.10 ± 0.2 | 3.16 ± 0.2 | 3.17 ± 0.2 | 3.08 ± 0.2 |
| LVPW; d (mm) | 2.75 ± 0.2[#] | 2.82 ± 0.4[#] | 3.00 ± 0.2[#] | 2.45 ± 0.2[#] | 2.46 ± 0.2[#] | 3.02 ± 0.2[*$#] |
| LVPW; s (mm) | 4.45 ± 0.2[#] | 4.35 ± 0.2[#] | 4.54 ± 0.2[#] | 4.17 ± 0.2 | 4.20 ± 0.2 | 4.64 ± 0.2[*$#] |
| EF (%) | 87 ± 2 | 88 ± 2 | 87 ± 4 | 88 ± 2 | 88 ± 4 | 87 ± 2 |
| FS (%) | 57.9 ± 3.2 | 59.3 ± 2.2 | 58.1 ± 4.4 | 59.2 ± 1.0 | 60.4 ± 4.8 | 58.0 ± 1.0 |
| SV (µL) | 247 ± 40 | 295 ± 12 | 257 ± 28 | 283 ± 30 | 311 ± 12 | 253 ± 40 |
| CO (mL/min) | 86 ± 12[#] | 104 ± 4 | 83 ± 8[#] | 101 ± 6 | 111 ± 6 | 89 ± 12[#] |
| E/A Ratio | 1.87 ± 0.3 | 1.38 ± 0.2[*#] | 1.62 ± 0.3[*$#] | 1.89 ± 0.3 | 1.95 ± 0.3 | 1.44 ± 0.2[*$#] |
| DT (ms) | 14.3 ± 0.2[#] | 20.6 ± 2.2[*#] | 14.5 ± 0.8[$#] | 13.7 ± 0.6[#] | 12.5 ± 0.6 | 17.8 ± 1.9[*$#] |
| BP (mmHg) | - | - | 137 ± 16 | - | - | 139 ± 12 |
| BW (g) | - | - | 718 ± 22[#] | - | - | 715 ± 42[#] |
| SubQ Fat (g) | - | - | 83 ± 24[#] | - | - | 86 ± 16[#] |
| RetroP Fat (g) | - | - | 44 ± 4[#] | - | - | 51 ± 8[#] |
| HW (mg) | - | - | 1878 ± 24[#] | - | - | 1735 ± 76 |
| HW/TL | - | - | 43.9 ± 0.8[#] | - | - | 41.0 ± 1.6[#] |
| Lung Weight/TL | - | - | 38.7 ± 1.2 | - | - | 42 ± 3.2 |

Data are shown as Mean ± SD. Data was analyzed by repeated measures of two-way ANOVA. Significance was determined by Tukey's post hoc test. * $p < 0.05$ compared to 16 wks within group, $ indicates $p < 0.05$ compared to 24 wks within group, # indicates $p < 0.05$ compared lean to age-matched obese ZSF1 rats; 4 animals per each group. HR, heart weight; LV, left ventricle; LVAW, left ventricle anterior wall thickness at end diastole (d) or end systole (s); LVID, left ventricular internal diameter at end diastole (d) or end systole (s); LVPW, left ventricle posterior wall thickness at end diastole (d) or end systole (s); EF, ejection fraction; FS, fraction shortening; SV, stroke volume; CO, cardiac output; E/A ratio, peak velocity of early/late mitral inflow ratio; DT, deceleration time; BP, blood pressure; BW, body weight; SubQ Fat, subcutaneous fat; RetroP Fat, retroperitoneal fat; HW, heart weight; TL, tibia length; - indicates no data was collected.




**Supplementary Figure 1.** RT-qPCR analysis for adeonsine A1, A2A, A2B and A3 receptor mRNA expression in skeletal muscle artery at 20 weeks of age in lean and obese ZSF1 rats (n=5-6 in each group).