SUPPLEMENTARY INFORMATION

Dendrimer-conjugated glutaminase inhibitor selectively targets microglial glutaminase in a mouse model of Rett syndrome

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1. Compound characterization:

Figure S1. $^1$H NMR of compound 3.
Figure S2. ESI-MS spectrum of compound 3.
Figure S3. $^1$H NMR of compound 4.
Figure S4. ESI-MS spectrum of compound 4.
Figure S5. $^1$H NMR of compound 6 (D-JHU29).

Figure S6. HPLC chromatogram of compound 6 (D-JHU29).
Figure S7. The zeta potential distribution of D-JHU29.

Figure S8. Flow cytometry gating scheme. Approximately $8.0 \times 10^4$ GFP+ and GFP- cells were collected per sample. Events were processed at a rate of 6,000 events/s and with a threshold count of $16.3 \times 10^6$. 

Neg = 74,699
Threshold Count = $16.3 \times 10^6$
6,000 evts/s
FSC & SSC = 1.0
Figure S9. Non-motor phenotypic assessments in MeCP2-KO mice after twice weekly D-JHU29 treatment. A. Neurobehavioral assessment is significantly greater in MeCP2-KO mice indicating significant phenotypic changes in these mice and there is no significant improvement with treatment. B. The predominant neurobehavior subscore, paw clench also shows no improvement change with D-JHU29 treatment. C. Respiration rate is significantly decreased in MeCP2-KO mice (gray bars) but is not recovered with D-JHU29 administration (blue bars). D. No improvements in novel object recognition were observed at D-JHU29 treatment. Only wild type (WT) mice (white bars) show on average more time spent with the novel object than what would be expected at chance (50%). *p < 0.05, ** p < 0.01
Neurobehavior Rubric:

Neurobehavioral phenotype was scored using the following measures by a blinded observer. All subscores were added to create an overall/composite neurobehavior score.

Subscore:

**Mobility**
- 0 normal, active
- 1 decreased spontaneous movement
- 2 no spontaneous movement, only moves when prodded
- 3 no movement

**Gait**
- 0 walks normally
- 1 waddling
- 2 waddling, walks on toes (paws not flat on ground)
- 3 waddling, feet displaced outward, paws clenched when walking

**Tremors**
- 0 none
- 1 sporadic
- 2 intermittent
- 3 continuous

**Paw Clenching**
- 0 none
- 1 1-2 paws
- 2 3 paws or both fore limbs/hind limbs
- 3 all paws

**Clench time**
- 0 none
- 1 sporadic
- 2 intermittent (patterned)
- 3 continuous

**Paw wringing**
- 0 none
- 1 some front paw
- 2 some front and back paw
- 3 continuous

**Respiration**
- 0 regular
- 1 irregular
- 2 too fast or too slow
- 3 apnic

**Composite Score**: addition of all sub-scores