THE FORCE™ PLATFORM ACHIEVES ROBUST KNOCKDOWN OF TOXIC HUMAN NUCLEAR DMPK RNA AND FOCI REDUCTION IN DM1 CELLS AND IN NEWLY DEVELOPED hTTR1/DMSXL MOUSE MODEL

STEFANO ZANOTTI, CODY DESJARDINS, NELSON HSIA, TIMOTHY WEEDE, RYAN J. RUSSO, LYDIA SCHLEEFKE, MONICA YAO, AYUN YE, SCOTT HILDEBRAND, JOHN NAJIM, QIFENG QIU, BRENDAN QUINN, KIM TANG, MO QATANANI, ROMESH SUBRAMANIAN, OXANA BESKROVNA

Dyne Therapeutics Inc., Waltham, MA, USA

RESULTS

- Reduces toxic human DMPK RNA
- Targets the genetic driver of DM1, namely human DMPK
- Corrects Foci
- Leads to sustained KD of toxic nuclear human DMPK

ACKNOWLEDGMENT

Editorial assistance, funded by Dyne Therapeutics, provided by Alicia Salinero, PhD, of JB Ashtin.

We thank Dr. Geneviève Gourdon for providing the DMSXL mice.

REFERENCES

CONCLUSIONS

- We designed a FORCE conjugate to address the genetic basis of DM1 by targeting the toxic CUG repeat transcript of DMPK
- These data demonstrated that our FORCE conjugate can:
  - Correct the DM1 phenotype of patient-derived myoblast cultures with a range of repeats, including those representative of severe DM1
  - Reduce toxic human DMPK foci in cardiac muscle of hTTR1/DMSXL mice
  - Lead to sustained KD of toxic human DMPK in hTTR1/DMSXL mice after a single dose
- These data strongly support further development of our FORCE conjugate, including a planned clinical study

DISCLOSURE INFORMATION

All authors are employees or shareholders of Dyne Therapeutics Inc. and may hold Dyne stock and/or stock options.

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