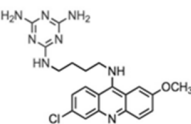
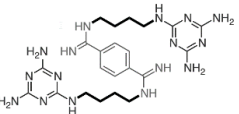
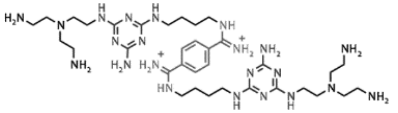
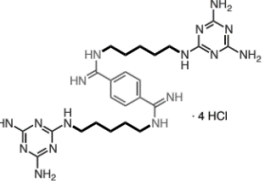
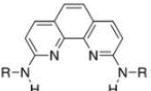
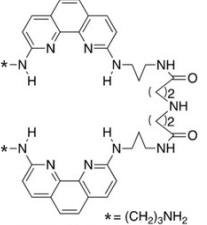
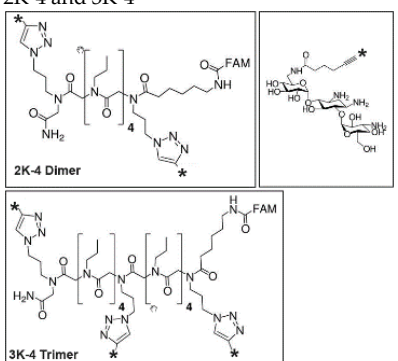
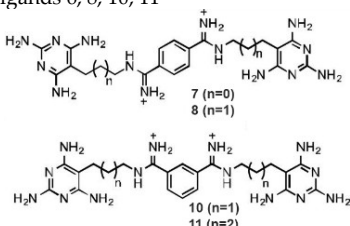
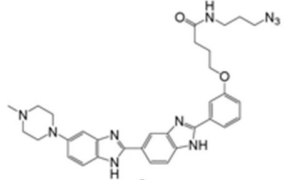
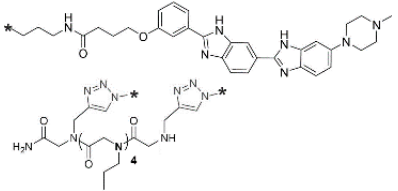
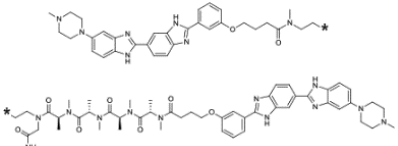
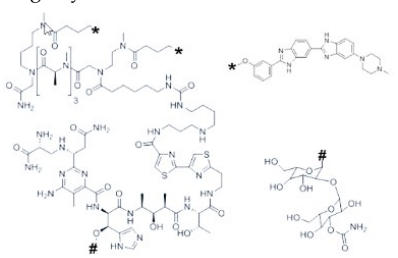


TABLE 1. Small molecules that target the toxic RNA through rational design.

COMPOUND ¹ STRUCTURE ²	MODEL ³	ACTIVE CONC. ⁴	OBSERVATION ⁵
Ligand 1 	MBNL1:r(CUG) _{4/12}	~50uM	CUG-MBNL1 complex disruption
Ligand 3 	MBNL1:r(CUG) ₁₂ DM1 HeLa cell	~10uM 50-100uM	CUG-MBNL1 complex disruption Foci reduction, minigene mis-splicing rescue
(New) Ligand 9 	(CTG-CAG) ₇₄ r(CUG) ₁₆ DM1 HeLa cell	50-100uM 5-100uM 25-150uM	Transcription inhibition Cleaved hairpin structure Foci reduction, minigene mis-splicing rescue, reduced r(CUG) _{exp} levels
Ligand 4 	(CTG-CAG) ₇₄ r(CUG) ₁₆ DM1 HeLa cell	0.05-0.4uM 0.2-4uM	Transcription inhibition Cooperative binding Foci reduction, minigene mis-splicing rescue, reduced r(CUG) _{exp} levels
DAP 	r(CUG) ₉ or r(CAG) ₉ d(CUG) ₂₀ luciferase reporter	25uM	Higher binding affinity for r(CUG) ₉ Decrease luciferase expression
DDAP 	r(CUG) ₉ or r(CAG) ₉ MBNL1:r(CUG) ₂₀ DM1 C2C12 cell DM1 HSA ^{LR} mouse	30-120nM 10-200nM 10-40uM 20 or 50mg/kg	Higher binding affinity for r(CUG) ₉ CUG-MBNL1 complex disruption Mis-splicing rescue Mis-splicing rescue
2K-4 and 3K-4 	MBNL1:r(CCUG) ₂₄ DM2 C2C12 cell	8-50nM 5-20uM	CCUG-MBNL1 complex disruption Minigene mis-splicing rescue

Ligands 6, 8, 10, 11  7 (n=0) 8 (n=1) 10 (n=1) 11 (n=2)	MBNL1:r(CCUG) ₈ DM2 HeLa cell	15-75uM 100uM	CCUG-MBNL1 complex disruption Foci reduction
Bis-benzimidazole 	MBNL1:r(CUG) ₁₀₉	110uM	CUG-MBNL1 complex disruption
2H-4  4	MBNL1:r(CUG) ₁₀₉ DM1 HeLa cell	11uM 5-25uM	CUG-MBNL1 complex disruption Minigene mis-splicing rescue, foci reduction
2H-K4NMeS 	MBNL1:r(CUG) ₁₂ DM1 patient-derived cell	10nM	CUG-MBNL1 complex disruption Foci reduction, mis-splicing rescue
Cugamycin  3 #	DM1 patient-derived cell DM1 HSA ^{L-R} mouse	1-4uM 10mg/kg	Foci reduction, mis-splicing rescue Foci reduction, mis-splicing rescue, myotonia rescue

¹ Name of compound.

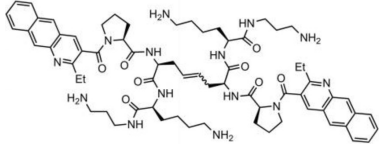
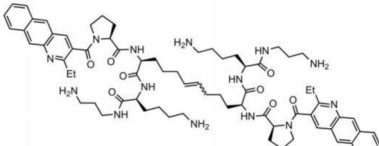
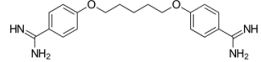
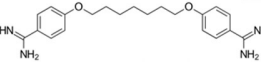
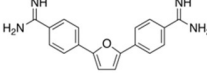
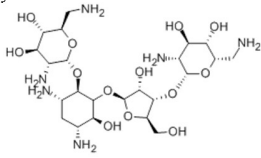
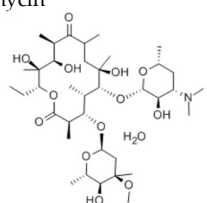
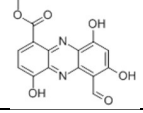
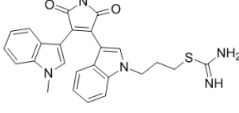
² Chemical structure of compound.

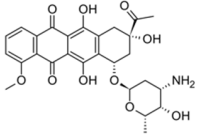
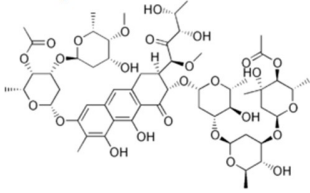
³ *In vitro* or *in vivo* model used.

⁴ Concentrations/ranges or doses where effect was observed in DM model (micromolar concentrations or mg/kg of body weight doses).

⁵ Observations of compound effect on DM molecular pathogenesis or phenotypes in DM model used.

TABLE 2. Small molecules identified via screens that target toxic CUG RNA.

COMPOUND ¹ STRUCTURE ²	MODEL ³	ACTIVE CONC. ⁴	OBSERVATION ⁵
Compound 4 	MBNL1::r(CUG) ₁₀₉ DM1 HSA ^{LR} mouse	1-100uM 40mg/kg	CUG-MBNL1 complex disruption Mis-splicing rescue
Compound 11 	MBNL1::r(CUG) ₁₀₉ DM1 HSA ^{LR} mouse	1-100uM 40mg/kg	CUG-MBNL1 complex disruption Mis-splicing rescue
Pentamidine 	DM1 HeLa cell (CTG-CAG) ₅₄ DM1 HSA ^{LR} mouse	10-75uM 10-100uM 25-40mg/kg	Foci reduction, minigene mis-splicing rescue, reduced r(CUG) _{exp} levels Transcription inhibition Mis-splicing rescue
Heptamidine 	DM1 HeLa cell DM1 HSA ^{LR} mouse	5-15uM 25-40mg/kg	Minigene mis-splicing rescue Mis-splicing rescue, reduced r(CUG) _{exp} levels, myotonia rescue
Furamidine 	MBNL1::r(CUG) ₄ DM1 HeLa cell DM1 patient-derived cell	10-125uM 20-80uM 0.25-4uM	CUG-MBNL1 complex disruption Foci reduction, mis-splicing rescue Foci reduction, mis-splicing rescue, rescued gene expression, increase MBNL1/2 protein levels
	DM1 HSA ^{LR} mouse	10-30mg/kg	Mis-splicing rescue, rescued gene expression, reduced r(CUG) _{exp} levels
Neomycin 	MBNL1::r(CUG) ₁₀₀	4-64uM	CUG-MBNL1 complex disruption
Erythromycin 	MBNL1::r(CUG) ₁₀₀ DM1 C2C12 cell DM1 patient-derived cell DM1 HSA ^{LR} mouse	4-64uM 50uM 25-100uM 150-900mg/kg	CUG-MBNL1 complex disruption Foci reduction, mis-splicing rescue Foci reduction, mis-splicing rescue Mis-splicing rescue, myotonia rescue
Lomofungin 	MBNL1::r(CUG) ₁₂ DM1 fluc800 cell	0.01-1uM 10uM	CUG-MBNL1 complex disruption Increased nucleoplasmic MBNL1 levels
	DM1 C2C12 cell	10uM	Mis-splicing rescue
Ro 31-8220 	DM1 patient-derived cell DM2 patient-derived cell DM1 Zebrafish	5-10uM 5-10uM 5uM	Foci reduction, mis-splicing rescue, downregulation of CELF1 levels, increased cytoplasmic levels of MBNL Foci reduction, increased cytoplasmic levels of MBNL Body length phenotype rescue

	DM1 heart-specific mouse	6mg/kg	Improved cardiac conduction and contractile abnormalities, mis-splicing rescue
APB1 peptide Ac-ppyawe-NH ₂ [*]	DM1 Drosophila	40-250uM	Increased muscle area, rescued eye and muscle degeneration, foci reduction
	DM1 HSA ^{LR} mouse	0.5 or 10ug	Mis-splicing rescue, increased Clcn1 expression, reduced central nuclei
Daunorubicin 	MBNL1:τ(CUG) ₂₆	10uM	CUG-MBNL1 complex disruption
	DM1 patient-derived cell	3-10uM	Foci reduction
	DM1 Drosophila	1uM	Rescued cardiac dysfunction, increased survival, foci reduction, mis-splicing rescue
Chromomycin A3 	DM1 patient-derived cell	0.04-4uM	Foci reduction, mis-splicing rescue, downregulation of CELF1 levels, increased cytoplasmic levels of MBNL
	DM1 patient-derived cell	0.04-4uM	Foci reduction, increased cytoplasmic levels of MBNL

¹ Name of compound.

² Chemical structure of compound.

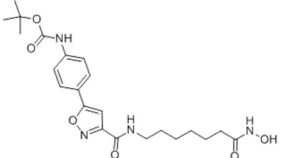
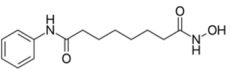
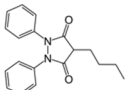
³ *In vitro* or *in vivo* model used.

⁴ Concentrations/ranges or doses where effect was observed in DM model (micromolar concentrations or mg/kg of body weight doses).

⁵ Observations of compound effect on DM molecular pathogenesis or phenotypes in DM model used.

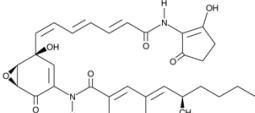
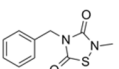
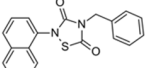
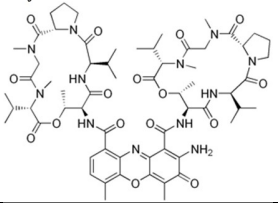
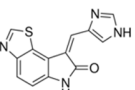
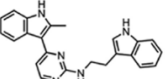
*Represents the lower case one-letter code for D-amino acids.

TABLE 3. Small molecules that upregulate MBNL protein levels.

COMPOUND ¹ STRUCTURE ²	MODEL ³	ACTIVE CONC. ⁴	OBSERVATION ⁵
ISOX 	MBNL-tag HeLa cell DM1 patient-derived cell	1-6uM 5uM	Increased MBNL1 protein levels Increased MBNL1 protein levels, mis-splicing rescue
Vorinostat 	MBNL-tag HeLa cell DM1 patient-derived cell	1-6uM 5uM	Increased MBNL1 protein levels Increased MBNL1 protein levels, mis-splicing rescue
Phenylbutazone (PBZ) 	C2C12 cell DM1 HSA ^{1R} mouse	50-950uM 16.7mg/kg	Increased <i>Mbnl1</i> expression Increased Mbnl1 protein levels, mis-splicing rescue, improved grip strength, reduction of central nuclei

¹ Name of compound.
² Chemical structure of compound.
³ *In vitro* or *in vivo* model used.
⁴ Concentrations/ranges or doses where effect was observed in DM model (micromolar concentrations or mg/kg of body weight doses).
⁵ Observations of compound effect on DM molecular pathogenesis or phenotypes in DM model used.

TABLE 4. Small molecules that affect downstream signaling pathways or restore CUGBP1 activity.

COMPOUND ¹ STRUCTURE ²	MODEL ³	ACTIVE CONC. ⁴	OBSERVATION ⁵
Manumycin A 	DM1 C2C12 cell DM1 HSA ^{LR} mouse	10-40uM	Mis-splicing rescue Mis-splicing rescue
Lithium Li ⁺	DM1 HSA ^{LR} mouse	0.24% diet	Improved grip strength, reduced central nuclei, myotonia rescue
TDZD-8 	DM1 HSA ^{LR} mouse	10mg/kg	Improved grip strength, myotonia rescue
Tideglusib 	Phase II clinical trials	400mg, 1000mg	Safety and efficiency
Actinomycin D 	DM1 HeLa cell DM1 patient-derived cell DM1 HSA ^{LR} mouse	0.005-0.02uM 5-10nM 1.25-2.5mg/kg	Foci reduction, reduction of r(CUG) _{exp} levels Reduced r(CUG) _{exp} levels Mis-splicing rescue
C-16 	DM1 patient-derived cell	1uM	Downregulation of CELF1, foci reduction, mis-splicing rescue
C-51 	DM1 patient-derived cell	30uM	Downregulation of CELF1, foci reduction, mis-splicing rescue

¹ Name of compound.

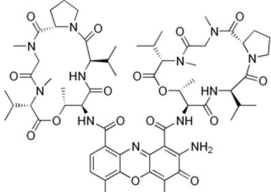
² Chemical structure of compound.

³ *In vitro* or *in vivo* model used.

⁴ Concentrations/ranges or doses where effect was observed in DM model (micromolar concentrations or mg/kg of body weight doses).

⁵ Observations of compound effect on DM molecular pathogenesis or phenotypes in DM model used.

TABLE 5. Small molecules that block transcription of the CTG expansion.

COMPOUND ¹ STRUCTURE ²	MODEL ³	ACTIVE CONC. ⁴	OBSERVATION ⁵
Actinomycin D 	DM1 HeLa cell DM1 patient-derived cell DM1 HSA ^{LR} mouse	0.005-0.02uM 5-10nM 1.25-2.5mg/kg	Foci reduction, reduction of r(CUG) _{exp} levels Reduced r(CUG) _{exp} levels Mis-splicing rescue

¹ Name of compound.

² Chemical structure of compound.

³ *In vitro* or *in vivo* model used.

⁴ Concentrations/ranges or doses where effect was observed in DM model (micromolar concentrations or mg/kg of body weight doses).

⁵ Observations of compound effect on DM molecular pathogenesis or phenotypes in DM model used.