Targeted oligo therapy for DM1

Dyne Therapeutics
Dyne’s Mission

Life-transforming therapies for patients with serious muscle diseases
Pioneering Targeted Therapies for Muscle Diseases

Genetic Muscle Diseases

Oligonucleotide Therapeutic

Targeted Delivery to Muscle
Dyne FORCE Platform: Antibody-Oligo Therapeutic

**Antibody**
- Initial focus: muscle-specific anti-TfR1
- Optimized for internalization

**Linker**
- Precise conjugation
- Circulating stability
- Endosomal release

**Oligo**
- Matched to target biology
- Specificity/low off targets
- Chemistry & design

Myotonic
FORCE Achieves Durable KD with Single Dose vs. Repeated Exposures Required for Naked ASO

- High potency
- High tolerability and duration of effect through 28 days
- Broad distribution to multiple muscle types

Myotonic

Source: Data based on published company reports. NHP data assumes NHP weight of 3 kg. KD: knockdown
Dyne-101 Significantly Decreases DMPK RNA In vivo dose-dependent target DMPK RNA knockdown

WT mice, n=5, single dose IV, 7 day study

Dose A: low dose
Dose B: high dose

* <0.05
** < 0.01
*** < 0.001

Myotonic
Dyne-102 Significantly Decreases DMPK RNA
Robust knock-down seen in NHP skeletal, smooth and cardiac muscles

WT NHP, n=3, single dose IV, 14 day study

Gastrocnemius
- DMPK vs PBS (Mean +/- 95% CI)
- PBS
- ASO
- Dyne-102

Soleus
- DMPK vs PBS (Mean +/- 95% CI)
- PBS
- ASO
- Dyne-102

Heart - left ventricle
- DMPK vs PBS (Mean +/- 95% CI)
- PBS
- ASO
- Dyne-102

Diaphragm
- DMPK vs PBS (Mean +/- 95% CI)
- PBS
- ASO
- Dyne-102

KD percentages:
- Gastrocnemius: 62%
- Soleus: 39%
- Heart: 49%
- Diaphragm: 36%
**Platform Validation Demonstrated From In Vivo Studies**

Potency and tolerability demonstrated in murine & NHP studies

<table>
<thead>
<tr>
<th></th>
<th>Murine</th>
<th>NHP</th>
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<tbody>
<tr>
<td><strong>Potency</strong></td>
<td>✓ Dose-dependent DMPK RNA KD</td>
<td>✓ Cardiac, skeletal, smooth muscle DMPK RNA KD</td>
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<tr>
<td><strong>Muscle Tissue Specificity</strong></td>
<td>✓ Muscle-specific DMPK RNA KD</td>
<td>✓ Muscle-specific DMPK RNA KD</td>
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<tr>
<td><strong>Tolerability</strong></td>
<td>✓ Favorable safety profile</td>
<td>✓ CBC, LFTs in normal range</td>
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<tr>
<td><strong>Duration of Effect</strong></td>
<td>✓ Duration of effect beyond 28 days</td>
<td>Pending</td>
</tr>
<tr>
<td><strong>POM in DM1 Disease Model</strong></td>
<td>✓ DMSXL model</td>
<td>N/A</td>
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Advancing Lead DM1 Program Toward Human POC

Preclinical Studies to IND
- NHP pharmacology
- Dosing regimen and duration
- IND-enabling studies

Phase 1 to Human POC
- Natural history study
- Established clinical plan to achieve rapid POC

BLA to Accelerated Approval
- Mechanistic and functional biomarkers
Dyne’s Mission

REPAIRING MUSCLE
RECLAIMING NOW

Life transforming therapies for serious muscle diseases

• DM1
• DMD
• FSHD
Thank you!