2019 Myotonic Annual Conference

September 13-14, 2019

Philadelphia, PA

Myotonic

Targeted oligo therapy for DM1

Dyne Therapeutics

Dyne's Mission

Life-transforming therapies for patients with serious muscle diseases

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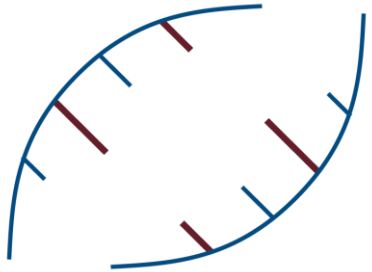
Dyne THERAPEUTICS

Pioneering Targeted Therapies for Muscle Diseases



Oligonucleotide Therapeutic

Genetic Muscle Diseases

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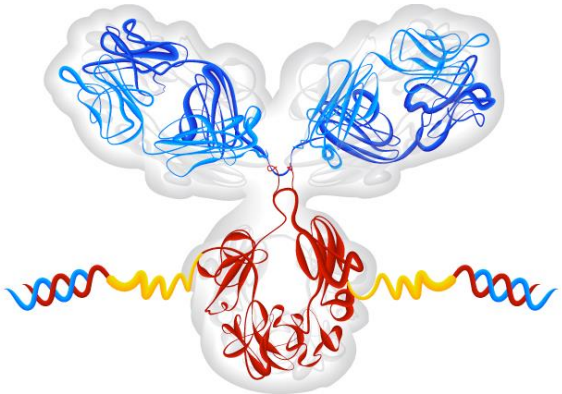

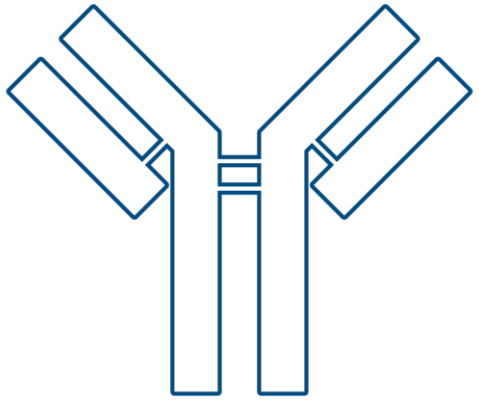

Targeted Delivery to Muscle

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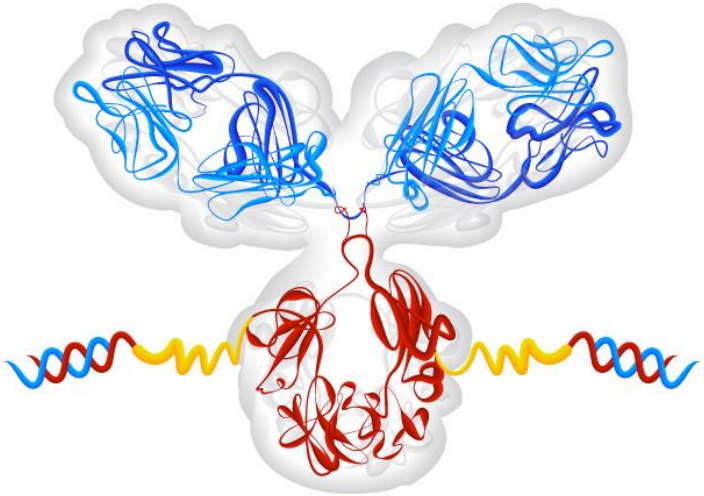
Dyne FORCE Platform: Antibody-Oligo Therapeutic



Manufacturing

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

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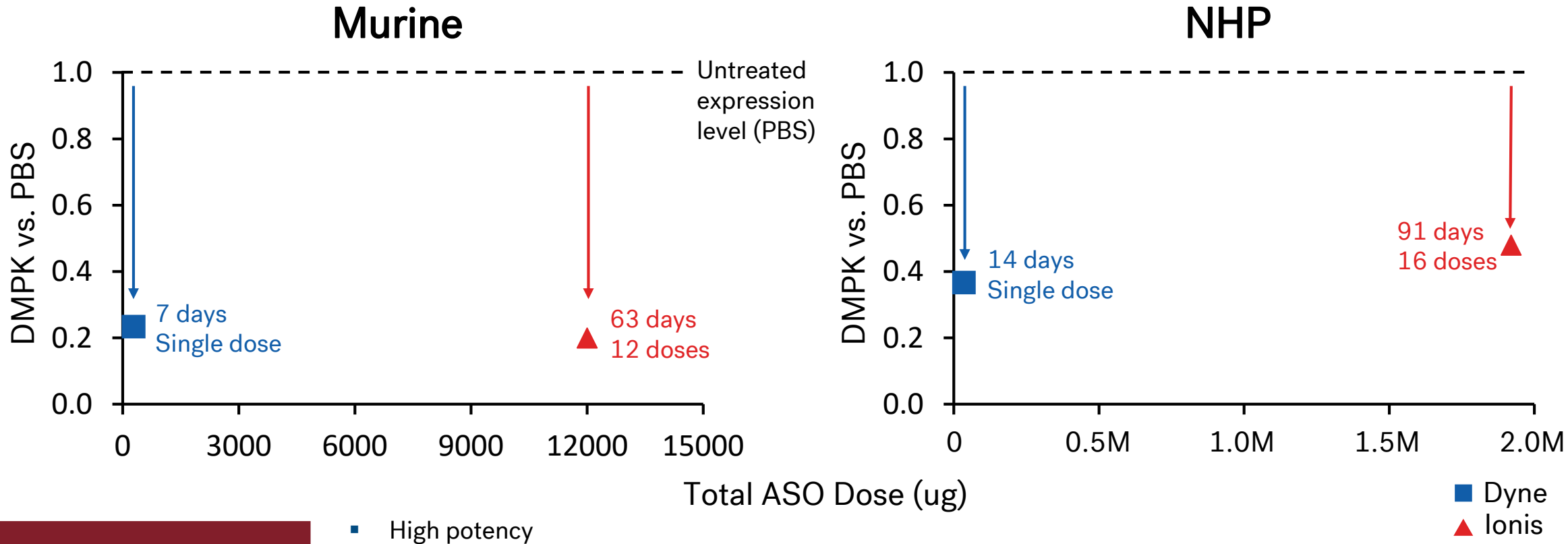
FORCE Achieves Durable KD with Single Dose vs. Repeated Exposures Required for Naked ASO



Dyne FORCE-DMPK

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

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Source: Data based on published company reports. NHP data assumes NHP weight of 3 kg. KD: knockdown

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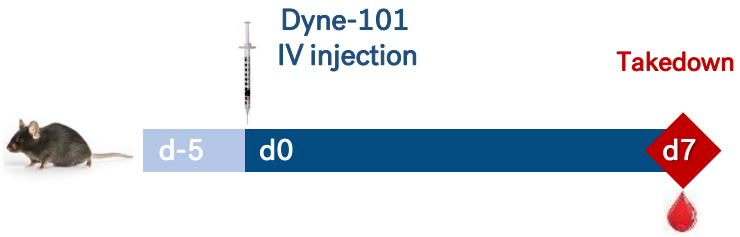
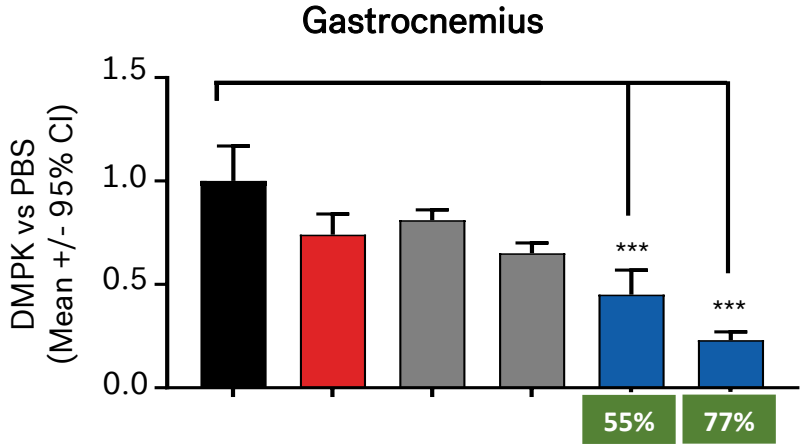
Dyne-101 Significantly Decreases DMPK RNA
In vivo dose-dependent target DMPK RNA knockdown

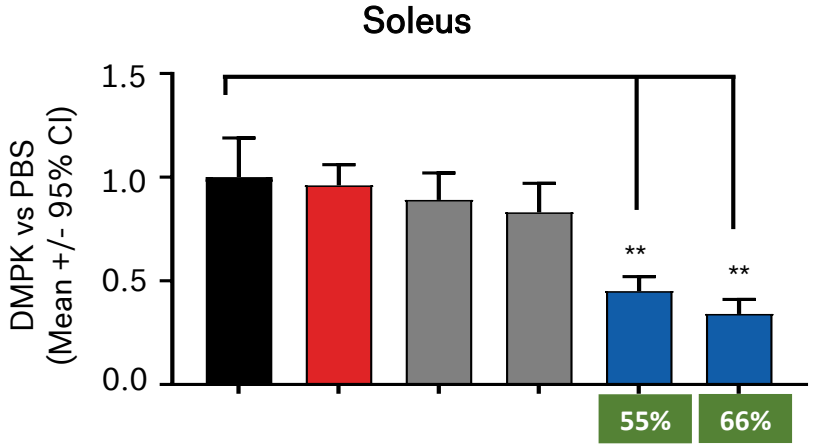


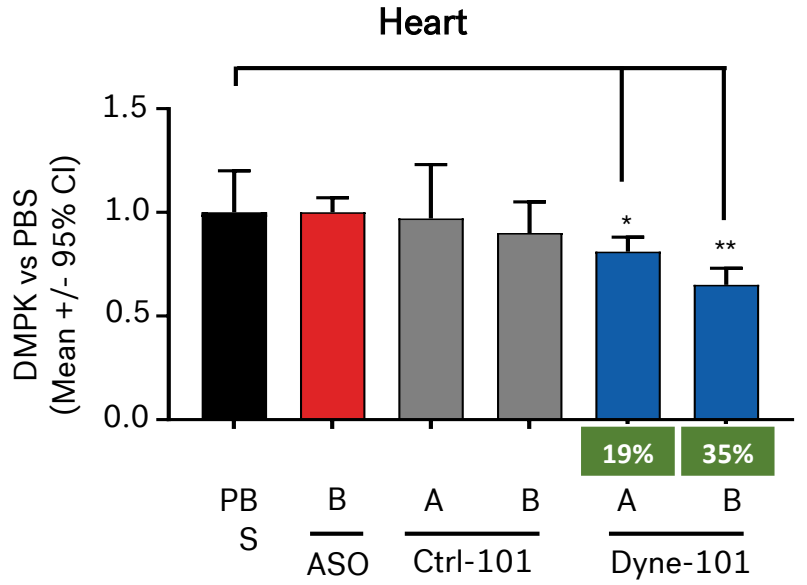
WT mice, n=5, single dose IV, 7 day study

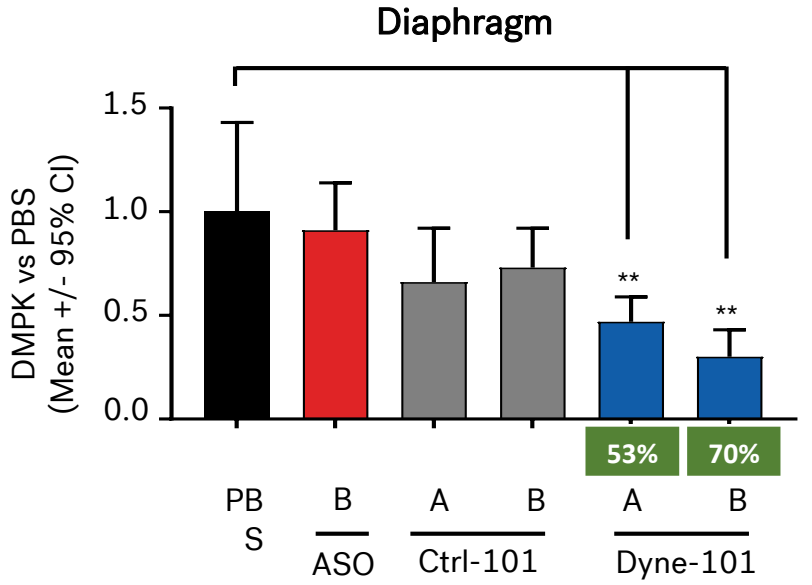
Dose A: low dose
Dose B: high dose

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









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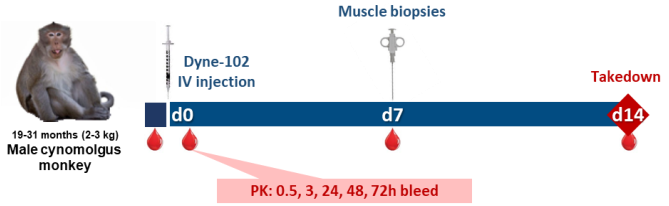
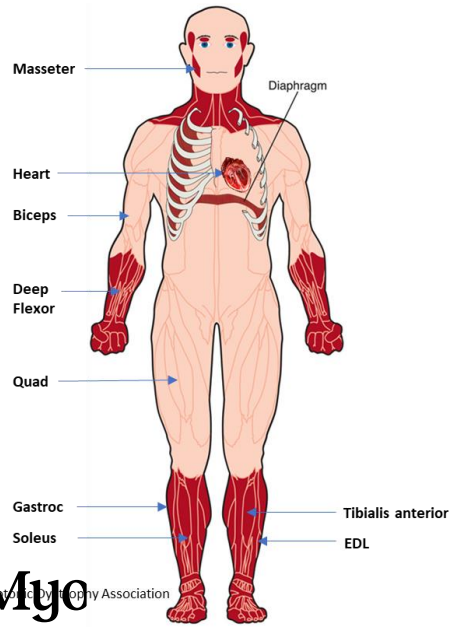
Dyne-102 Significantly Decreases DMPK RNA

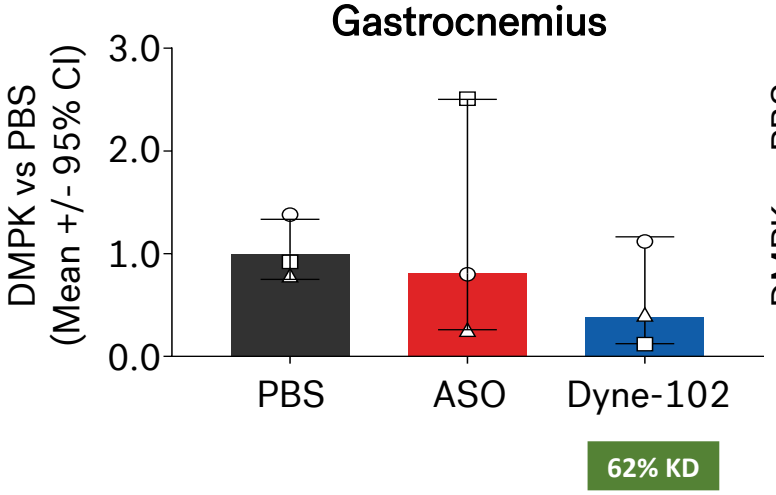
Robust knock-down seen in NHP skeletal, smooth and cardiac muscles

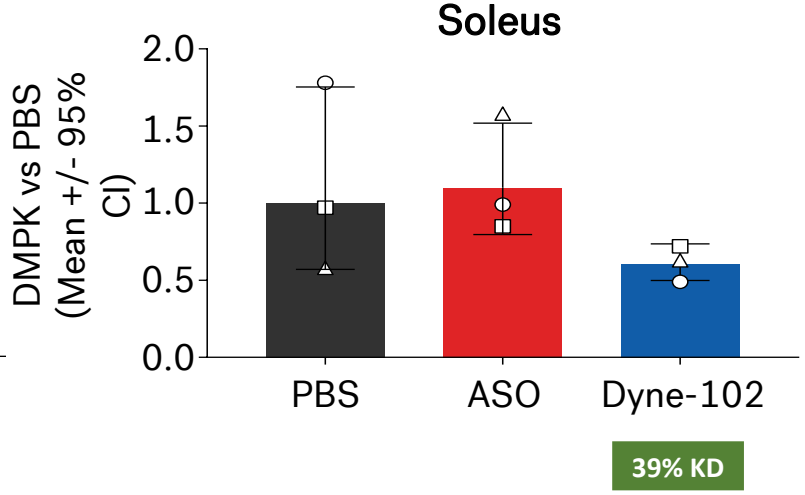


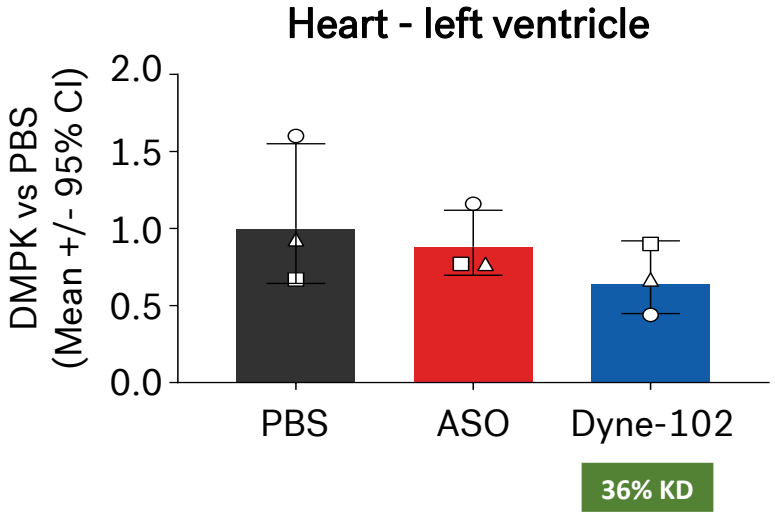
WT NHP, n=3, single dose IV, 14 day study

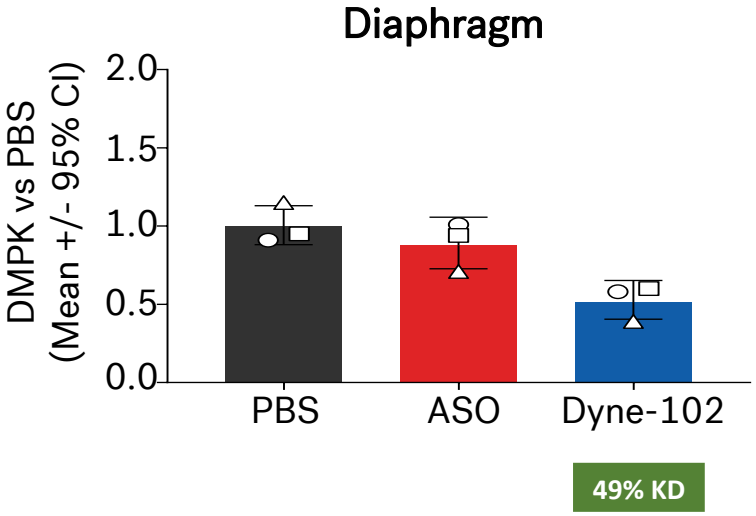


Source: Muscular Dystrophy Association









Platform Validation Demonstrated From In Vivo Studies
Potency and tolerability demonstrated in murine & NHP studies

	Murine	NHP
Potency	✓ Dose-dependent DMPK RNA KD	✓ Cardiac, skeletal, smooth muscle DMPK RNA KD
Muscle Tissue Specificity	✓ Muscle-specific DMPK RNA KD	✓ Muscle-specific DMPK RNA KD
Tolerability	✓ Favorable safety profile	✓ CBC, LFTs in normal range
Duration of Effect	✓ Duration of effect beyond 28 days	Pending
POM in DM1 Disease Model	✓ DMSXL model	N/A

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Dyne THERAPEUTICS

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

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Dyne THERAPEUTICS

Dyne's Mission

REPAIRING **MUSCLE**
RECLAIMING **NOW**

Life transforming therapies for serious muscle diseases

- DM1
- DMD
- FSHD

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Thank you!