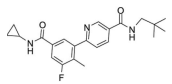
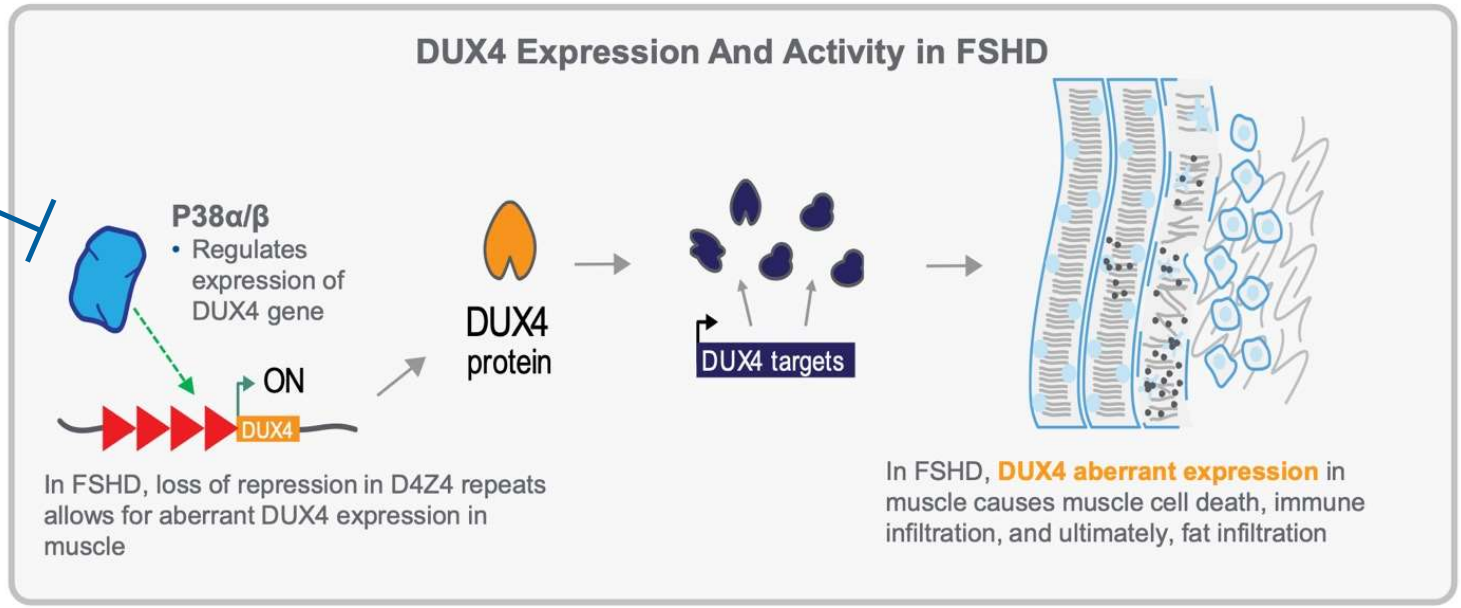
Fulcrum REACH Clinical Trial

Fulcrum Therapeutics



Losmapimod

Interfere with DUX4 transcription



Administration:

Other Notes:

- Repurposed drug
- No safety concerns in 3,600 previous study participants

https://www.fulcrumtx.com/wp-content/uploads/Annualized-Data-Presentation-MDA-Final_220408.pdf

REACH sponsored by Fulcrum Therapeutics

QUICK FACTS

Drug	Losmapimod
How is it given?	Pill, taken twice a day
Phase	3
Participants	260
Placebo	Yes, 1:1
Genetic Testing	Required, provided by study
Rx Duration	48 weeks
Study Visits	6 + screening and follow-up
Notable Activities	MRI
Open-Label Extension	Yes

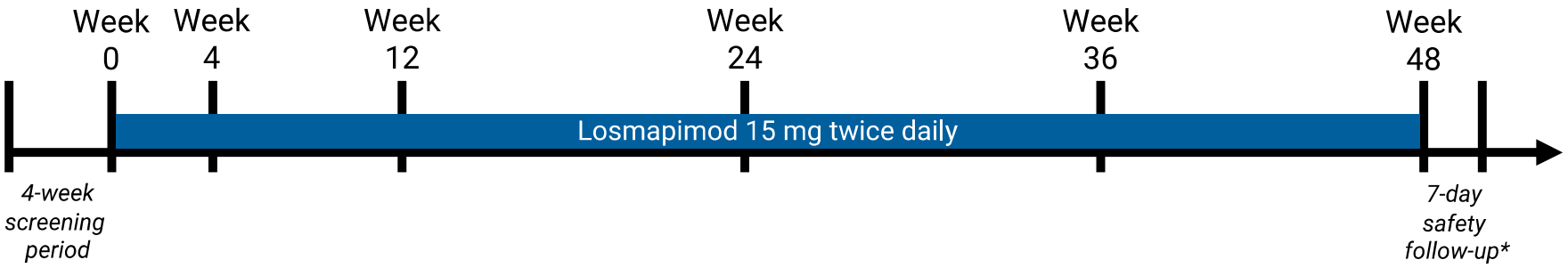
STATUS

Enrollment	Completed
Data Expected	Q4 2024
Locations	US, Canada, Denmark, France, Germany, Italy, Netherlands, Spain, UK
Learn More	*clinicaltrials.gov/study/NCT05397470* *fshdsociety.org/fulcrum-reach-trial*

WHO CAN PARTICIPATE

- Age 18-65
- FSHD1 or FSHD2
- Ricci score 2-4 (cannot be dependent on wheelchair or walker for activities)
- Reachable Workspace total RSA 0.2-0.7
- Must be able to do MRI

Fulcrum Therapeutics



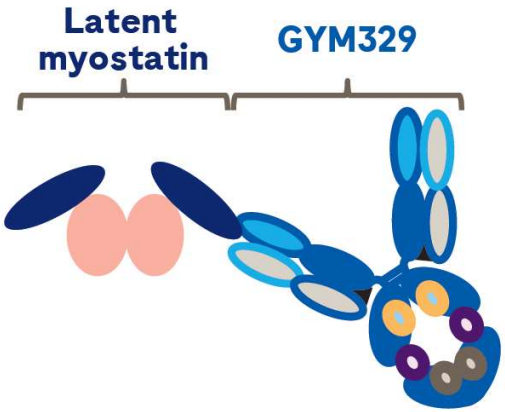
Roche MANOEUVRE Clinical Trial

Helps muscles grow

What is GYM329 and how does it work?

GYM329 is an investigational, anti-latent myostatin antibody that specifically binds to inactive latent myostatin[4]

- Myostatin is a negative regulator of muscle growth and acts to prevent muscular hypertrophy.[5]
- GYM329 specifically binds to inactive latent myostatin and blocks its conversion to active myostatin, an intervention that is hypothesized to lead to increased muscle growth.[4]
- Preclinical animal studies have demonstrated increases in muscle mass and strength following treatment with GYM329.[4]



Administration:

Other Notes:

- AKA RO7204239
- Next generation of anti-myostatin agents
- May require lower and less frequent dosing

https://medically.gene.com/content/dam/pdmahub/restricted/neurology/mda-2023/MDA-2023-poster-statland-MANOEUVRE-study-design-a-study-of-GYM329-RO7204239.pdf

MANOEUVRE sponsored by Hoffmann-La Roche

QUICK FACTS

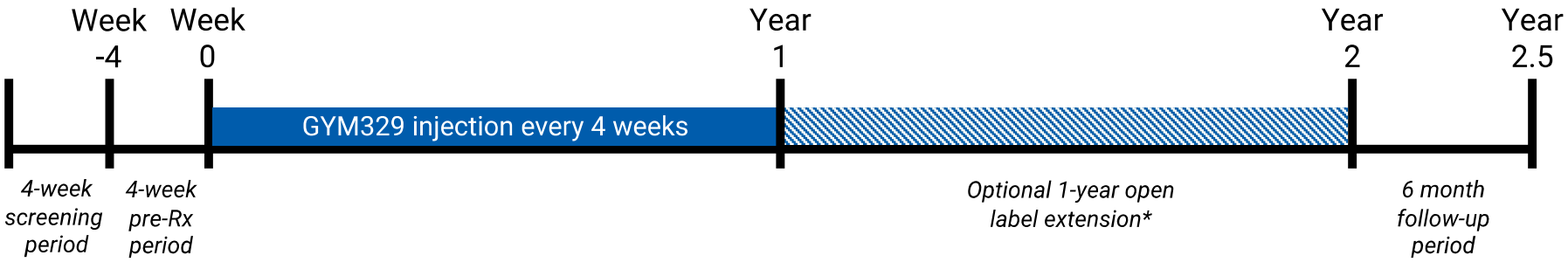
Drug	GYM329 (aka RO7204239)
How is it given?	Injection under skin
Phase	2
Participants	48
Placebo	Yes, 1:1
Genetic Testing	Required, talk to your local site
Rx Duration	Every 4 weeks for 52 weeks
Study Visits	At least every 4 weeks
Notable Activities	Wearable device, MRI
Open-Label Extension	Yes, for 52 weeks

STATUS

Enrollment	Currently enrolling
Data Expected	TBD
Locations	US, Denmark, Italy, UK
Learn More	*forpatients.roche.com* *clinicaltrials.gov/study/NCT05548556* *fshdsociety.org/roche-manoeuvre-trial/*

WHO CAN PARTICIPATE?

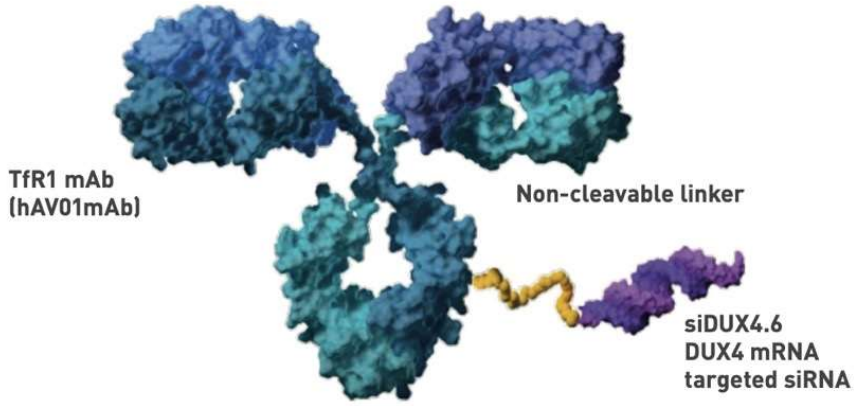
- Age 18-65
- FSHD1 or FSHD2
- Ricci score 2-4 (must be able to walk unassisted)
- Must be able to do MRI



Avidity FORTITUDE Clinical Trial

- **Figure 2** illustrates the structure of AOC 1020 and its three components:
  1. **Antibody:** Human transferrin receptor 1 (TfR1) targeting, effector function-null, humanized IgG1 antibody (hAVO1mAb) to affect delivery to skeletal muscle[7,8]
  2. **Non-cleavable linker:** MCC maleimide linker, enhanced for safety and durability[7,8]
  3. **Oligonucleotide:** Stabilized siRNA targeting DUX4 mRNA (siDUX4.6); engineered and stabilized to withstand lysosomal enzymes, selected for potency and specificity, and modified to diminish off-target effects[7,8]

Figure 2. AOC 1020: An antibody oligonucleotide conjugate targeting DUX4 mRNA for degradation



Remove DUX4 RNA

Administration:

Other Notes: Related drug in Myotonic Dystrophy (AOC 1001) was first ever AOC in clinic, performing favorably in Phase 1/2

https://www.aviditybiosciences.com/wp-content/uploads/2023/03/Fortitude-Poster_MDA-2023_FINAL.pdf

FORTITUDE sponsored by Avidity Biosciences

QUICK FACTS

Drug	AOC1020
How is it given?	Intravenous infusion
Phase	1/2a
Participants	72
Placebo	Yes, 2:1
Genetic Testing	Required, provided by study
Rx Duration	5 doses over 9 months
Study Visits	~20, some may be virtual
Notable Activities	MRI, leg muscle biopsy
Open-Label Extension	Yes

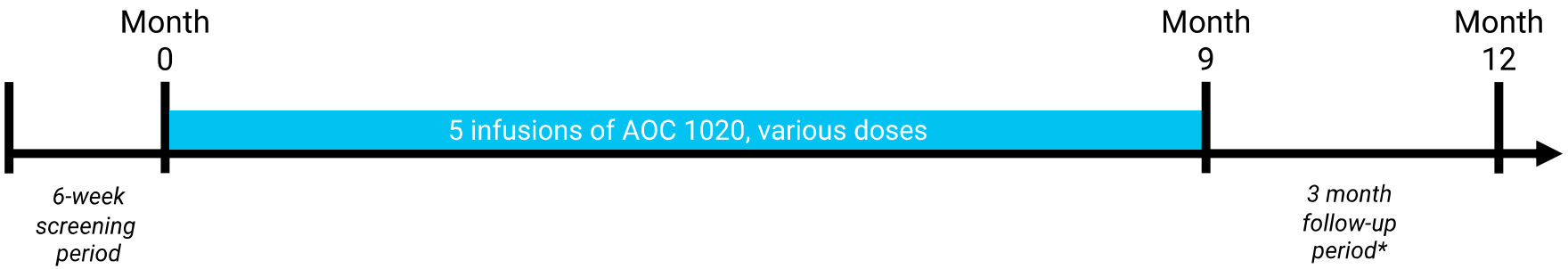
STATUS

Enrollment	Currently enrolling
Data Expected	Preliminary data Q2 2024
Locations	US, Canada, UK
Learn More	*fortitude-study.com* *clinicaltrials.gov/study/NCT05747924* *fshdsociety.org/avidity-fortitude-trial/*

WHO CAN PARTICIPATE?

- Age 18-65
- FSHD1 or FSHD2
- FSHD clinical score of 2-14
- Able to walk 10 meters without assistance
- Reachable Workspace score
- Must have leg muscle suitable for biopsy and be able to do MRI

AVIDITY BIOSCIENCES

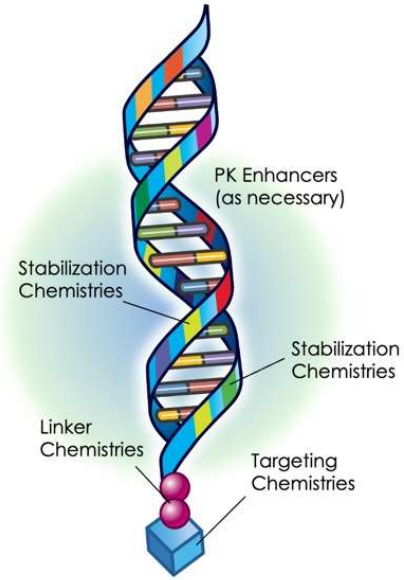


COMING SOON: Arrowhead ARO-DUX4 Trial

arrowhead pharmaceuticals

Remove DUX4 RNA

Arrowhead TRiM™ Platform for Muscle Diseases



Components:

- Unique sequence selection targeting the DUX4 gene
- Stabilization chemistries
- Linker chemistries
- Targeting ligands for muscle cells

Administration:

Other Notes: None

ARO-DUX4 trial sponsored by Arrowhead Pharmaceuticals

QUICK FACTS

Drug	ARO-DUX4
How is it given?	Intravenous injection
Phase	1/2a
Participants	52
Placebo	Yes, 3:1
Genetic Testing	Required, provided by study
Rx Duration	Part 1: duration 3 months Part 2: 2 or 4 doses over 1 year
Study Visits	~20
Notable Activities	MRI, leg muscle biopsy
Open-Label Extension	Yes

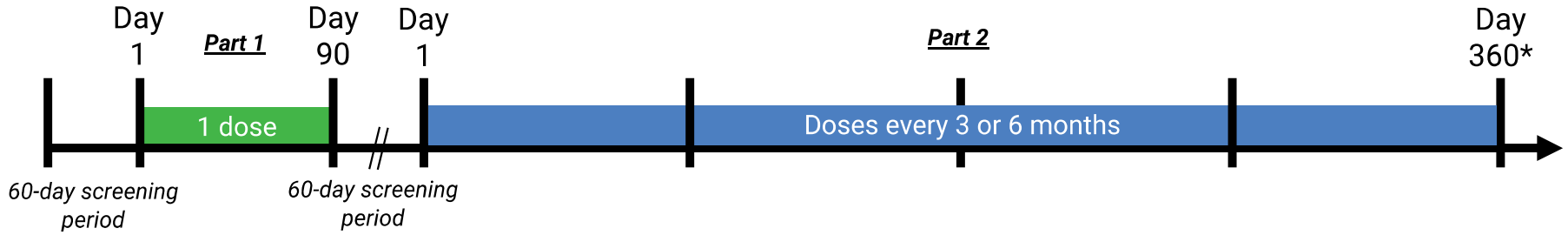
STATUS

Enrollment	Beginning early 2024
Data Expected	TBD
Locations	New Zealand, Canada (TBC)
Learn More	*fshdsociety.org/arrowhead-trial* *clinicaltrials.gov/study/NCT06131983*

WHO CAN PARTICIPATE?

- Age 18-70
- FSHD1
- Clinical Severity Scale 3-8
- Must have leg muscle suitable for biopsy and be able to do MRI

arrowhead pharmaceuticals



REINFORCE by Centre Hospitalier Universitaire de Nice, principal investigator Sabrina Sacconi, funded by Hoffmann-La Roche

QUICK FACTS

Drug	Satralizumab
How is it given?	Injection under skin
Phase	2
Participants	40
Placebo	Yes
Genetic Testing	Required
Rx Duration	Double-blind phase, at weeks 0, 2, 4, and every 4 weeks thereafter for 48 weeks; open-label phase, same dosing for 48 weeks; plus follow-ups. Total 116 weeks
Study Visits	~18
Notable Activities	MRI, blood draws
Open-Label Extension	Yes

STATUS

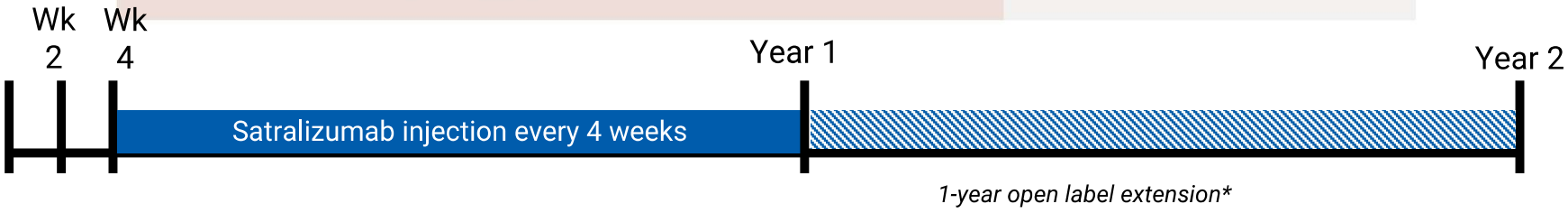
Enrollment	Beginning early 2024
Data Expected	After 2027
Locations	Ottawa, Canada; Nice, France
Learn More	*clinicaltrials.gov/study/NCT06222827*

WHO CAN PARTICIPATE?

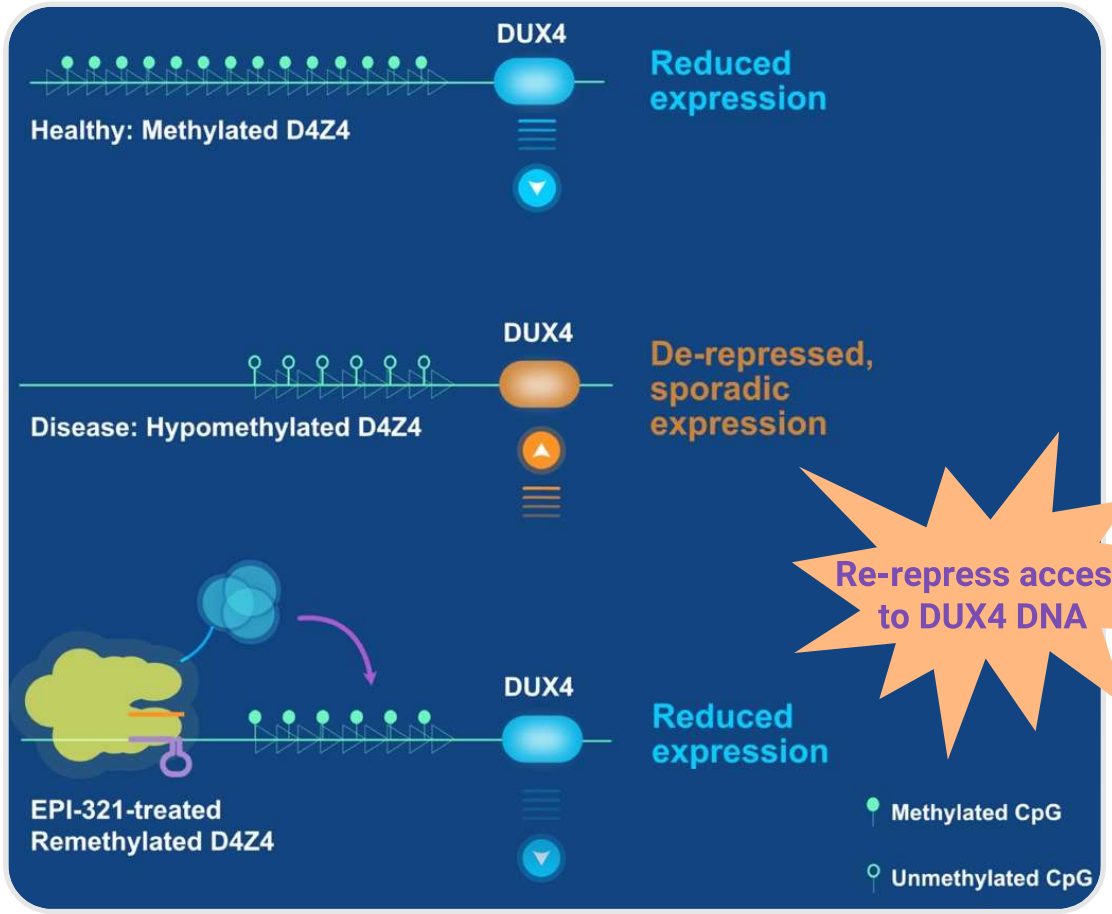
- Age 18-65
- FSHD1
- Ricci score 2-4, able to walk without support
- Must be able to do MRI

Roche

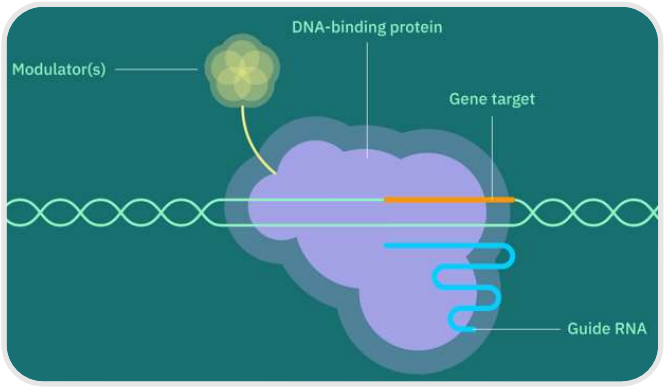
Centre Hospitalier Universitaire de Nice



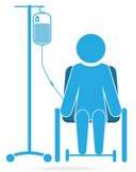
COMING SOON: Epic Bio



Re-repress access to DUX4 DNA



Administration:

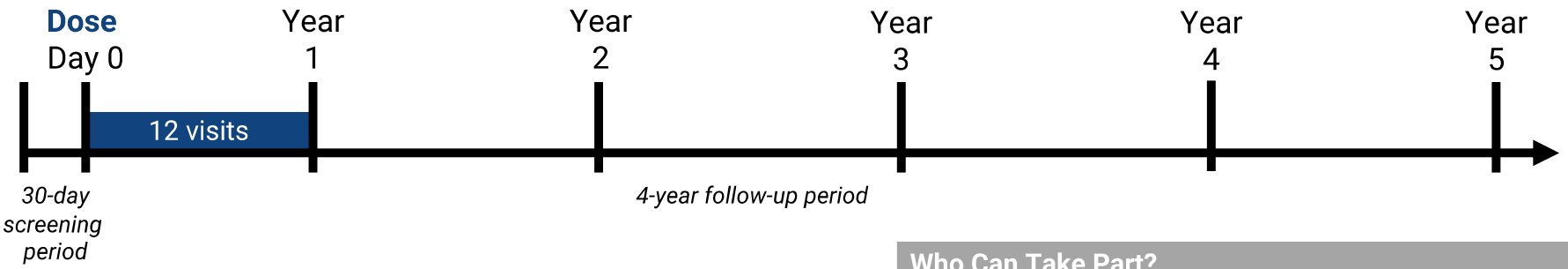


Other Notes:

- Expected to be long lasting, potentially even one-time
- Platform utilizes CRISPR-based technology

https://epic-bio.com/wp-content/uploads/2023/10/WMS2023-Final-Poster.pdf and https://epic-bio.com/science/

COMING SOON: Epic Bio



Quick Facts:	
Phase	1/2
Participants	~6-9
Placebo	No, all patients receive drug
Genetic Testing	Required
Rx Duration	1 dose
Study Visits	~12 over 1 year
Notable Activities	MRI, muscle biopsy
Open Label Extension	N/A

Who Can Take Part?
Age 18-75
FSHD1
Ricci score 2-4
Must be able to walk 10 meters
Must be able to do MRI

Get Involved:	
Enrollment	TBD in 2024
Data Expected	TBD
Locations	US, Canada, UK, Germany, Netherlands
Learn More	FSHD Society YouTube

Many more therapies coming down the pipeline!

Academic research labs working on drug discovery

Additional companies in ‘stealth’ mode