PepGen

PEPGEN REPORTS POSITIVE DATA FROM PHASE 1 TRIAL OF PGN-EDO51 FOR THE TREATMENT OF DUCHENNE MUSCULAR DYSTROPHY

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Chief Executive Officer

SEPTEMBER 28, 2022

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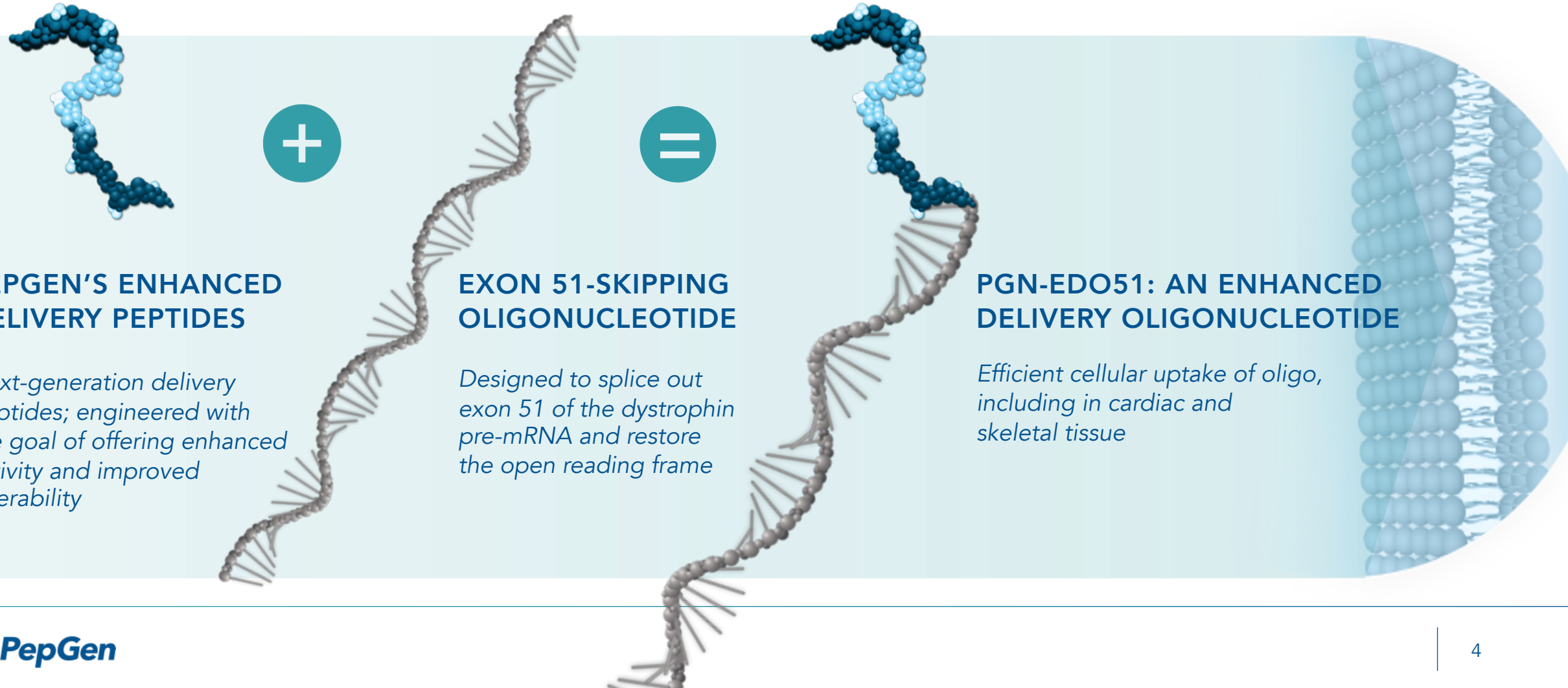
POSITIVE DATA FROM PGN-EDO51 PH1 SINGLE ASCENDING DOSE TRIAL

PGN-EDO51 Ph1 HNV trial overview	• A **double-blind, placebo-controlled single ascending dose trial** evaluating the safety and tolerability of PGN-EDO51 in 32 healthy adult males; tissue concentration and exon skipping were also assessed • Subjects were randomized to **1, 5, 10 or 15 mg/kg doses** of PGN-EDO51 or placebo • Following a **single IV administration** of PGN-EDO51, safety data were evaluated by a Safety Review Committee (SRC) prior to dose escalation
Trial results	• PGN-EDO51 was **generally well-tolerated at the doses assessed**, and was **more potent than anticipated** • We observed the **highest level of oligonucleotide delivery and exon 51 skipping in human muscle following a single dose*** • **Accumulation of exon 51-skipped transcript** was observed from day 10 to day 28, suggesting the potential for transcript and dystrophin accumulation in future repeat dose patient trials • The **oligonucleotide tissue concentrations observed in this trial were similar to those seen in PGN-EDODM1 preclinical studies at pharmacologically active dose levels**, supporting the clinical potential of PGN-EDODM1

*Comparative statements are based on cross-trial comparisons with publicly-available data for other exon skipping approaches that have been assessed following a single dose.

PGN-EDO51 LEVERAGES PEPGEN'S ENHANCED DELIVERY OLIGONUCLEOTIDE (EDO) TECHNOLOGY

PGN-EDO51 for the treatment of Duchenne muscular dystrophy (DMD) is a well-characterized investigational exon 51-skipping oligonucleotide conjugated to one of our proprietary delivery-enhancing peptides



PEPGEN'S ENHANCED DELIVERY PEPTIDES

Next-generation delivery peptides; engineered with the goal of offering enhanced activity and improved tolerability

EXON 51-SKIPPING OLIGONUCLEOTIDE

Designed to splice out exon 51 of the dystrophin pre-mRNA and restore the open reading frame

PGN-EDO51: AN ENHANCED DELIVERY OLIGONUCLEOTIDE

Efficient cellular uptake of oligo, including in cardiac and skeletal tissue

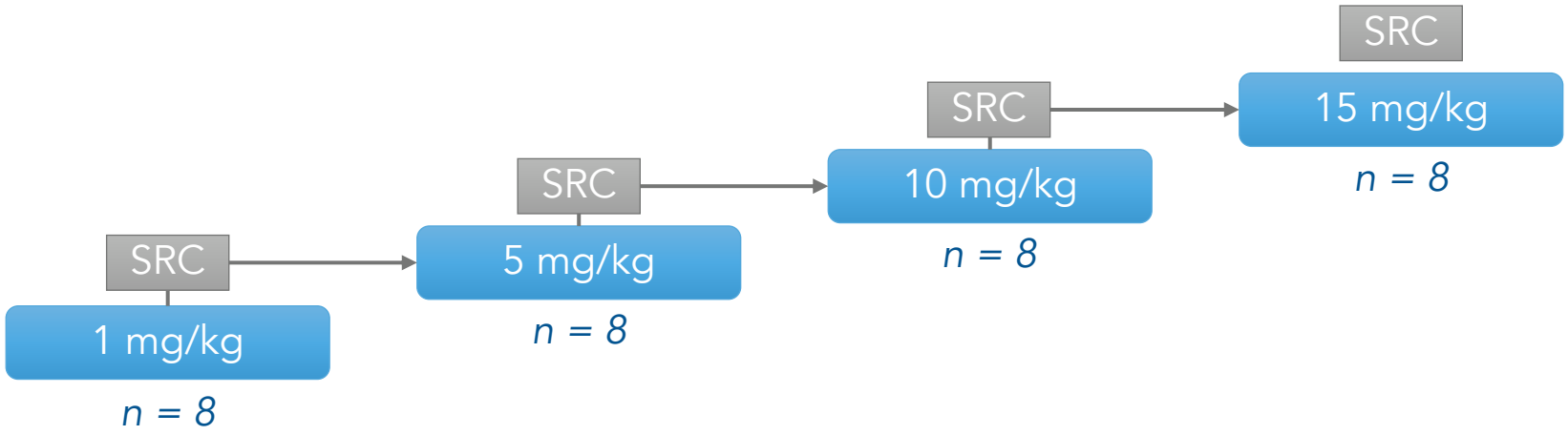
PGN-EDO51 FOR DUCHENNE MUSCULAR DYSTROPHY

Michelle Mellion, M.D.

SVP Clinical Development

WE HAVE COMPLETED A SINGLE ASCENDING DOSE PH1 TRIAL OF PGN-EDO51 IN HEALTHY NORMAL VOLUNTEERS

PH1 HEALTHY NORMAL VOLUNTEER (HNV) TRIAL SUMMARY

Overview	• **Study population:** Healthy adult males (n = 32, 3:1 PGN-EDO51:placebo) • **Dosing:** Single dose, i.v. administration • **Placebo control** • Biceps biopsies conducted on **Day 10 and Day 28**
Trial summary	

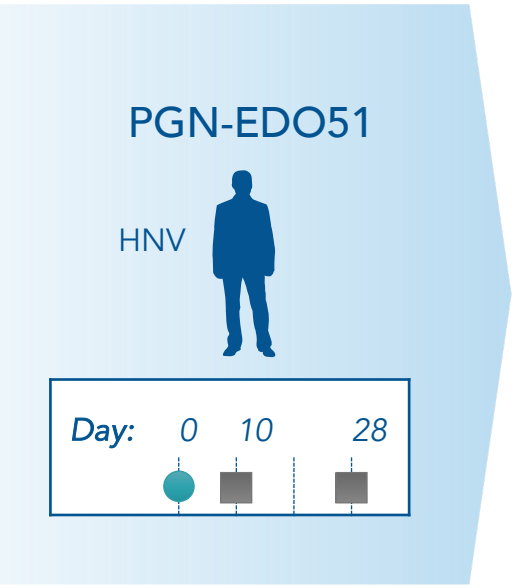
SRC = safety review committee.

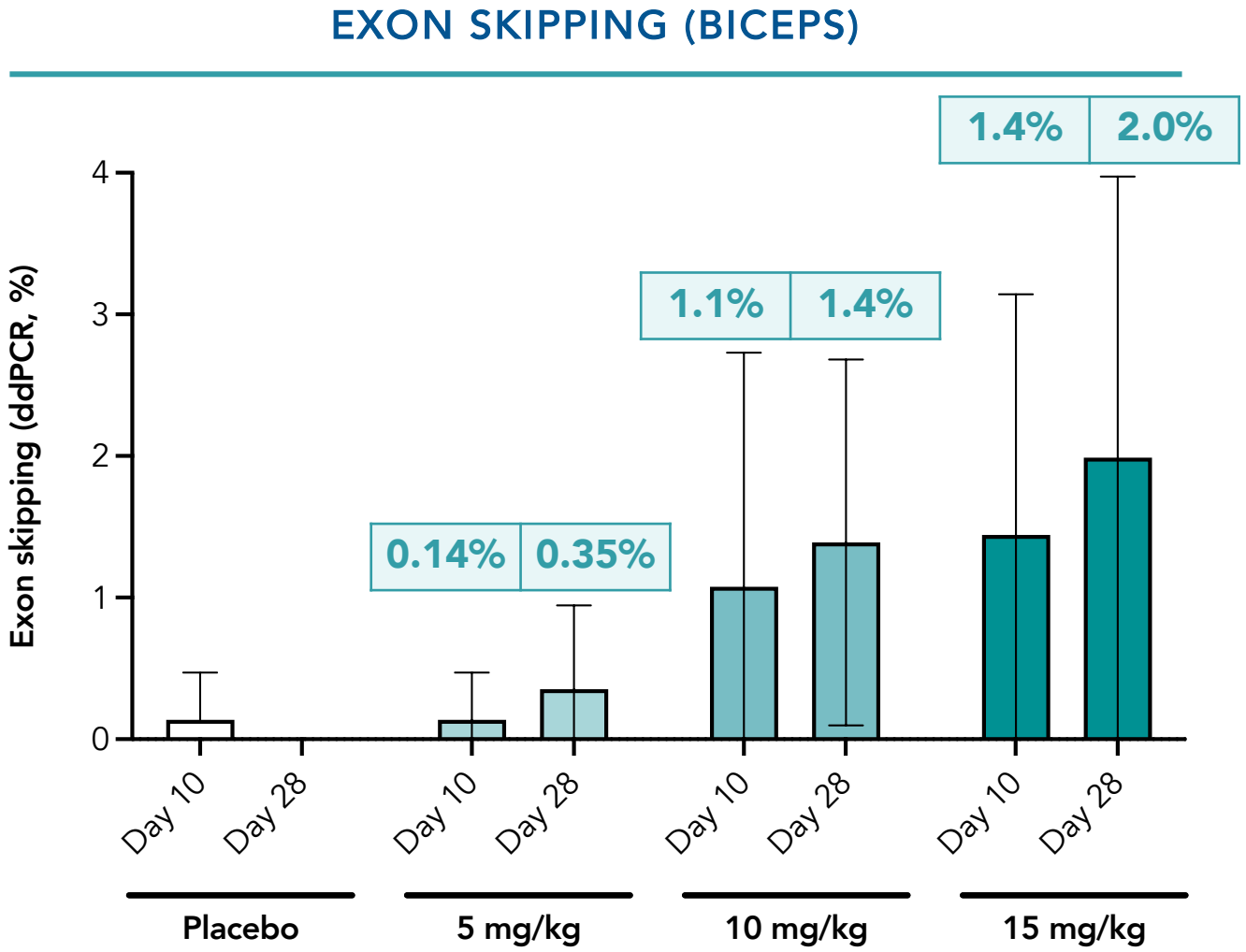
HIGHEST LEVELS OF OLIGO DELIVERY & EXON 51 SKIPPING OBSERVED, SUPPORTING FURTHER DEVELOPMENT OF PGN-EDO51

PH1 ENDPOINTS	READOUTS OBTAINED
Target engagement *Exon skipping (biceps)*	**Highest level of DMD exon 51 skipping** observed following a single dose in humans
Pharmacokinetics *Tissue concentration (biceps)*	**Highest level of oligonucleotide delivery** observed for a DMD therapeutic following a single dose in humans
Safety & tolerability	**Generally well-tolerated**

Comparative statements are based on cross-trial comparisons with publicly-available data for other exon skipping approaches that have been assessed following a single dose.

HIGHEST LEVELS OF EXON 51 SKIPPING OBSERVED IN HUMANS FOLLOWING A SINGLE DOSE





Protocol PGN-EDO51-101: Phase 1, first in human, randomized double blind, placebo controlled single ascending dose study in healthy adult volunteers. Single dose of either PGN-EDO51 or Placebo were administered by IV infusion at doses indicated. Participants were followed for 28 day period following dose administration to evaluate safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD). Needle biopsies of biceps muscle were taken on Day 10 and Day 28. Exon skipping measured by ddPCR. Shown as mean ± SD; n = 6 PGN-EDO51: 2 Placebo per cohort (n = 5 for D10 at 15 mg/kg). Comparative statements are based on cross-trial comparisons with publicly-available data for other exon skipping approaches that have been assessed following a single dose.

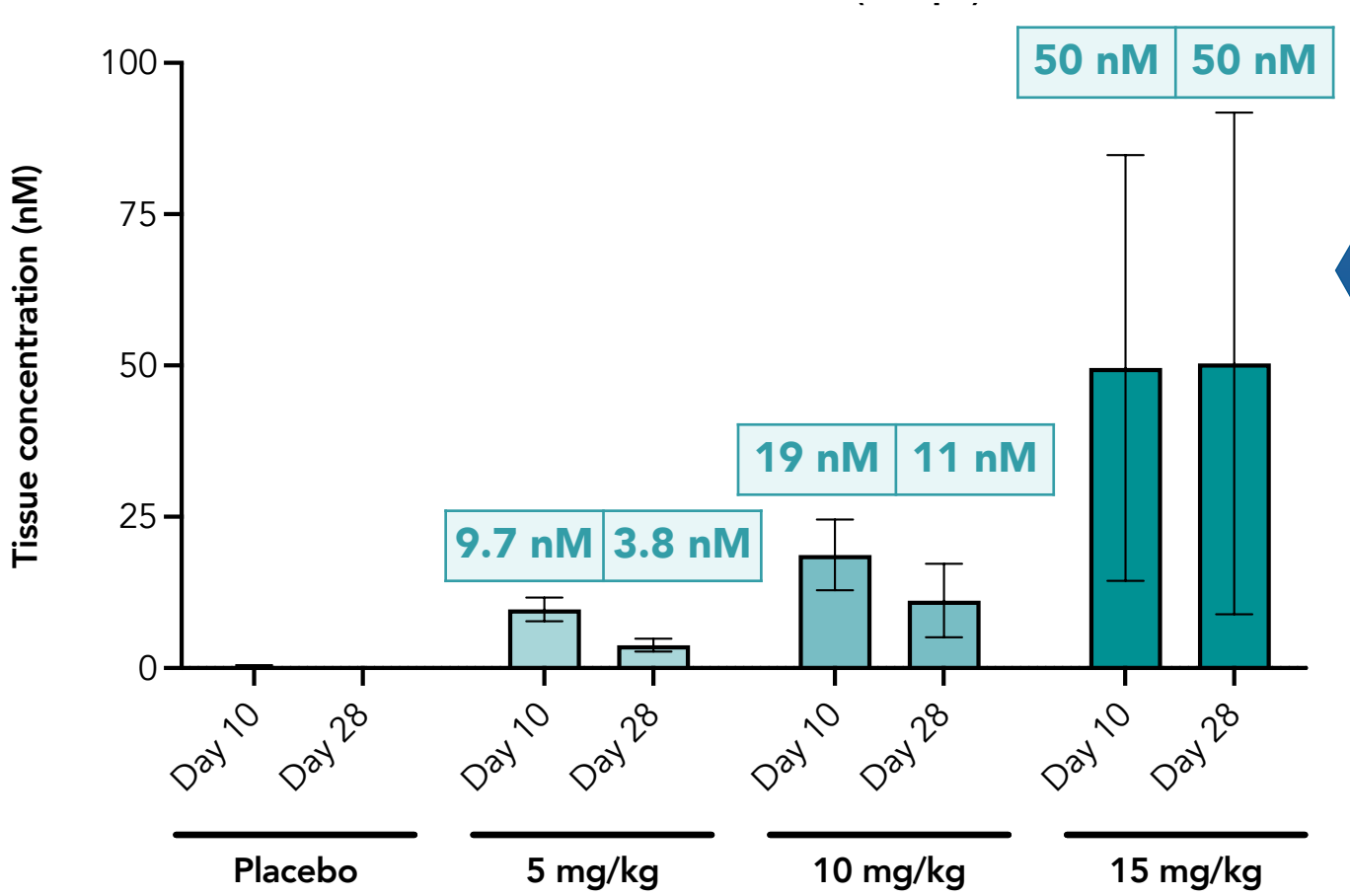
HIGH, PERSISTENT TISSUE CONCENTRATIONS OF OLIGONUCLEOTIDE WERE OBSERVED

PGN-EDO51

PGN-EDO51 dose

Biceps biopsy

TISSUE CONCENTRATION (BICEPS)



These results further support our belief that repeat dosing of PGN-EDO51 may lead to **accumulation of skipped transcript and dystrophin** following repeat dosing in DMD patients

Protocol PGN-EDO51-101: Phase 1, first in human, randomized double blind, placebo controlled single ascending dose study in healthy adult volunteers. Single dose of either PGN-EDO51 or Placebo were administered by IV infusion at doses indicated. Participants were followed for 28 day period following dose administration to evaluate safety, tolerability, PK, and PD. Needle biopsies of biceps muscle were taken on Day 10 and Day 28. Tissue concentration measured by ELISA. Shown as mean ± SD; n = 6 PGN-EDO51: 2 Placebo per cohort (n = 5 for D10 at 15 mg/kg).

PGN-EDO51 WAS GENERALLY WELL-TOLERATED AT DOSES ASSESSED IN PH1 SAD TRIAL

SAFETY & TOLERABILITY SUMMARY

- All participants completed the study; there were **no discontinuations**.
- The majority of treatment-emergent adverse events (TEAEs) were assessed as **mild and resolved without any intervention**. At 10 mg/kg there were **only Grade 1 (mild)** AEs .
- At 15 mg/kg there were **transient, reversible** changes in kidney biomarkers that **resolved in all subjects**.
- At 15 mg/kg there was one non-life threatening serious adverse event (SAE) related to changes in kidney biomarkers that were **transient and reversible**. This HNV was admitted to the hospital for less than 24 hours, received hydration and then was re-admitted to the Phase 1 unit and completed the study.
- Transient mild (Grade 1) to moderate (Grade 2) hypomagnesemia was observed in two participants at the 15 mg/kg dose and **did not require any intervention**.
- Serum cystatin C, the recommended biomarker to assess renal function in DMD, showed **minimal change at the highest dose**.

In light of higher than anticipated oligo levels and exon skipping levels in muscle observed at 5 mg/kg and 10 mg/kg , further does escalation was not deemed necessary by sponsor. Under this Phase 1 protocol any non-life-threatening SAE was considered a dose-limiting toxicity (DLT), however study was not halted by the SRC nor put on hold by Health Canada.

MAJORITY OF TEAEs MILD AND RESOLVED WITHOUT INTERVENTION; SUPPORTS PROGRESSION TO PH2a PATIENT TRIAL

PH1 TRIAL SAFETY & TOLERABILITY SUMMARY

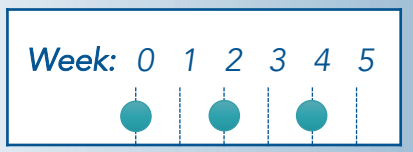
Healthy Normal Volunteers (HNV) with ≥1 AE, n (%)	Placebo (n=8)	Cohort A: 1 mg/kg (n=6)	Cohort B: 5 mg/kg (n=6)	Cohort C: 10mg/kg (n=6)	Cohort D: 15 mg/kg (n=6)	PGN-EDO51 Total (n=24)
Any AE	4 (50)	4 (66.7)	2 (33.3)	5 (83.3)	6 (100)	17 (70.8)
Related to study drug	1 (12.5)	2 (33.3)	0	4 (66.7)	6 (100)	12 (50)
Serious AE related to study drug	0	0	0	0	1 (16.7)	1 (4.2)
AE leading to discontinuation	0	0	0	0	0	0
AE leading to death	0	0	0	0	0	0
Number of Related TEAEs by CTCAE v5.0 grading*						
Grade 1 (Mild)	1	1	0	7	12	20
Grade 2 (Moderate)	0	1	0	0	3	4
Grade 3 (Severe)	0	0	0	0	1	1

* No Grade 4 or 5 recorded; Protocol PGN-EDO51-101: Phase 1, first in human, randomized double blind, placebo controlled single ascending dose study in healthy adult volunteers. Single dose of either PGN-EDO51 or Placebo were administered by IV infusion at doses indicated. Participants were followed for 28 day period following dose administration to evaluate safety, tolerability, PK, and PD.

IN NHP REPEAT DOSE STUDY, KIDNEY BIOMARKER ELEVATIONS WERE REDUCED AFTER FIRST DOSE OF PGN-EDO51

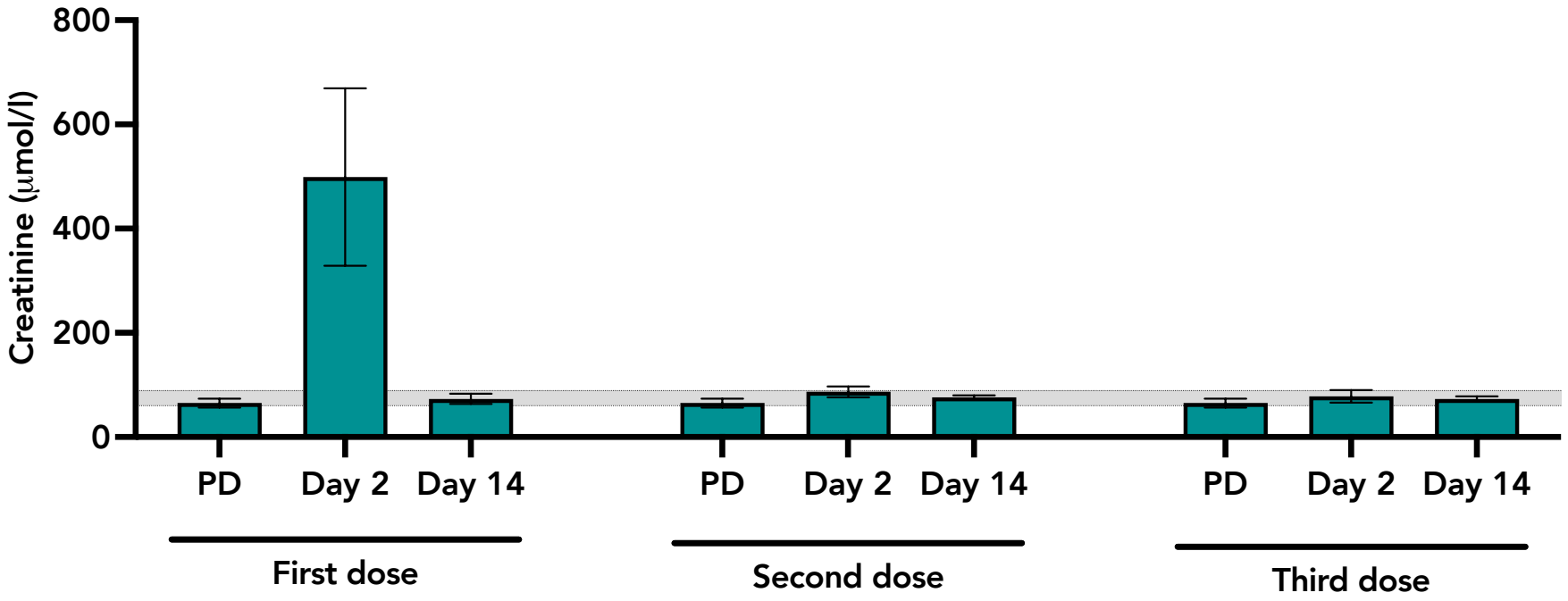
PGN-EDO51

WT



PPMO dose

REPEAT-DOSE SERUM CREATININE LEVELS *(HIGH-DOSE COHORT)*



These results support the potential tolerability of PGN-EDO51 with repeat dosing

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PD = pre-dose. Protocol: PGN-EDO51 was administered to NHP by IV infusion over 30 min at a given dose level (n=3). Q2W, three doses administered, saline control. Tissues were harvested 7 days after final administration. Shown as mean ± SD; n = 3 per group. Study was not powered for statistical significance. Grey bar shows normal range.

PEPGEN HAS COMPLETED A PH1 HNV TRIAL FOR PGN-EDO51; ON TRACK TO INITIATE DMD PATIENT CLINICAL TRIAL IN 1H23

	2022	2023	2024
Anticipated milestones	• **2Q:** First HNV dosed in Ph1 trial ✓ • **3Q: Ph1 clinical safety, oligo delivery & exon skipping data** ✓ • **4Q:** Completion of Ph2a-enabling tox studies	• **1H: Initiation of Ph2a DMD patient clinical trial**	• Safety and **dystrophin data** in DMD patients (Ph2a)
Overview	• Ph1 trial showed highest single-dose levels of exon skipping & oligo delivery • PGN-EDO51 was generally well-tolerated • We believe readouts support progression to Ph2a	• Trial will assess safety and tolerability, exon skipping and dystrophin in DMD patients • Safety readouts from HNV trial anticipated to support MAD initiation at higher dose levels • Precedents suggest that exon skipping readouts will be higher in patients than in HNVs at the same dose level • Anticipate trial will be conducted in multiple geographies, including U.S.	

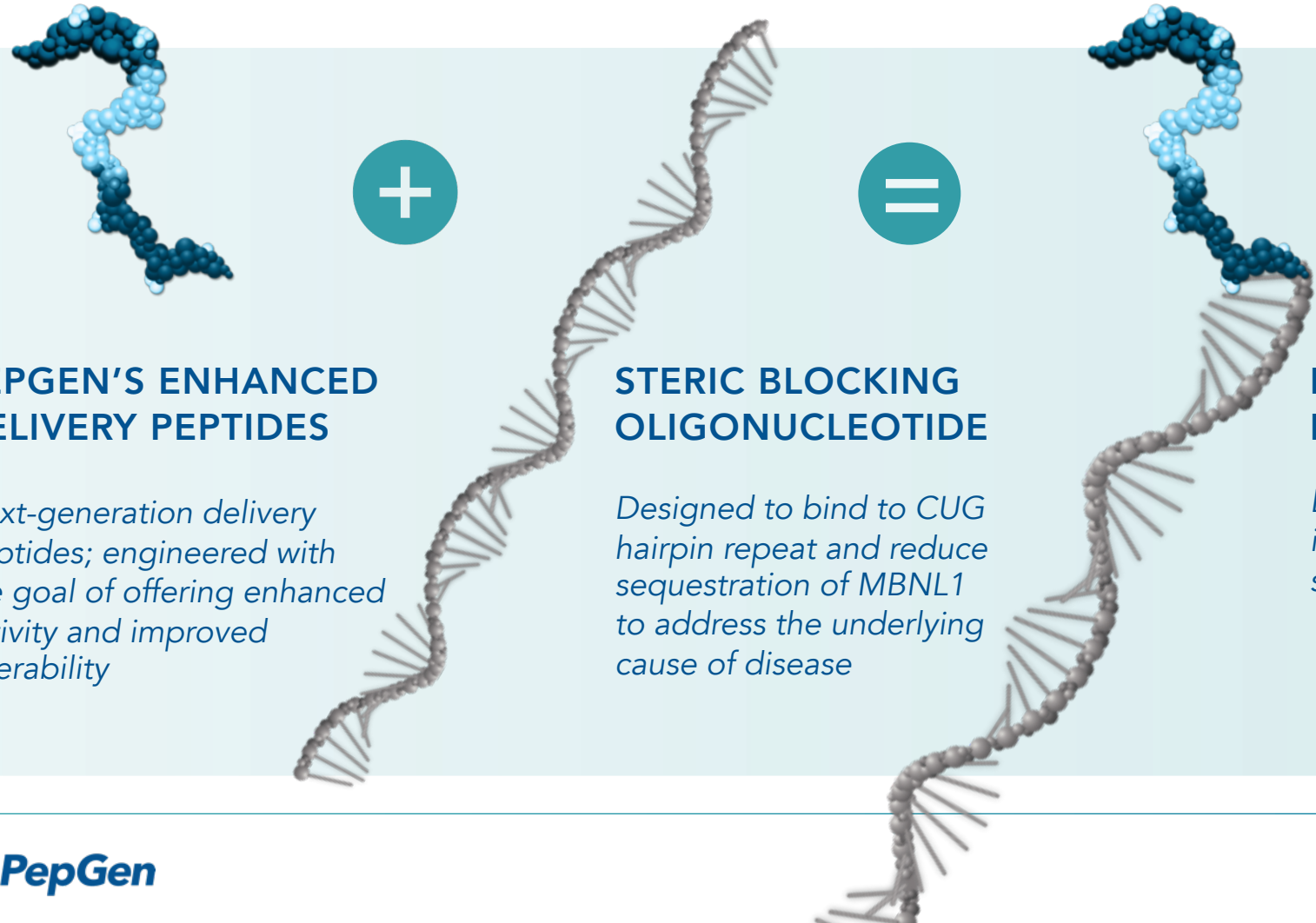
PGN-EDODM1 FOR MYOTONIC DYSTROPHY TYPE 1 (DM1)

Jaya Goyal, Ph.D.

EVP Research & Preclinical Development

PGN-EDO51 DATA SUPPORTS THE CLINICAL POTENTIAL OF PGN-EDODM1 FOR THE TREATMENT OF MYOTONIC DYSTROPHY TYPE 1

PGN-EDODM1 for the treatment of myotonic dystrophy type 1 (DM1) is a well-characterized investigational steric blocking oligonucleotide conjugated to one of our proprietary delivery-enhancing peptides



PEPGEN'S ENHANCED DELIVERY PEPTIDES

Next-generation delivery peptides; engineered with the goal of offering enhanced activity and improved tolerability

STERIC BLOCKING OLIGONUCLEOTIDE

Designed to bind to CUG hairpin repeat and reduce sequestration of MBNL1 to address the underlying cause of disease

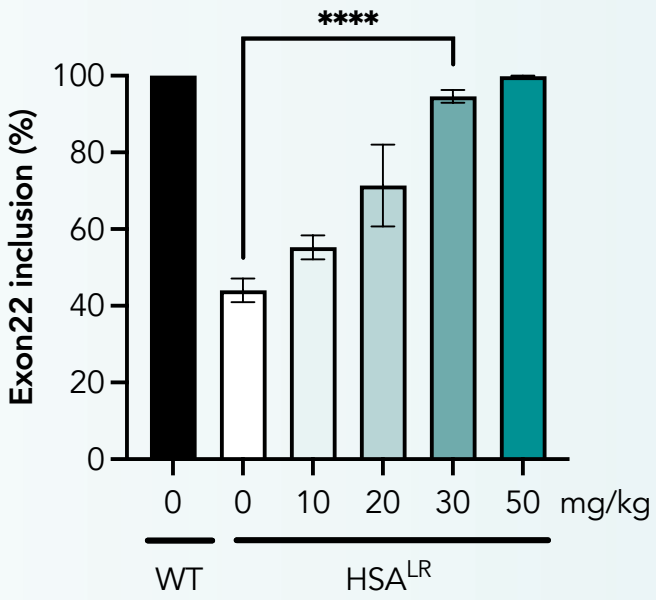
PGN-EDODM1: AN ENHANCED DELIVERY OLIGONUCLEOTIDE

Efficient cellular uptake of oligo, including in cardiac and skeletal tissue and the CNS

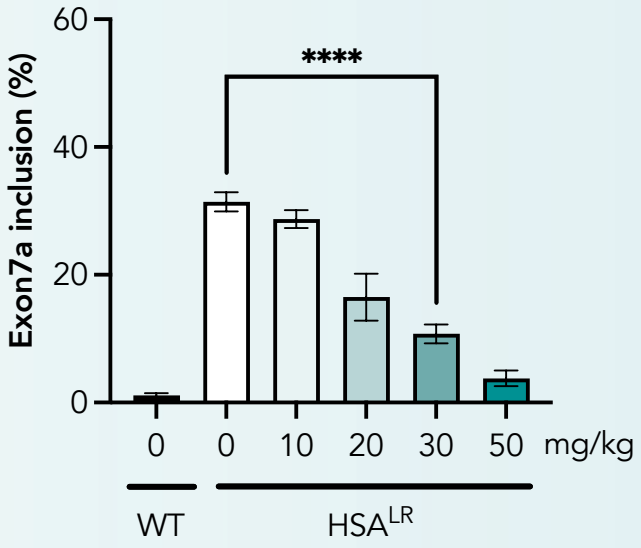
PGN-EDODM1 CORRECTED MOLECULAR AND FUNCTIONAL DM1 PHENOTYPE IN HSA^{LR} MOUSE

CORRECTION OF MIS-SPLICING

Atp2a1

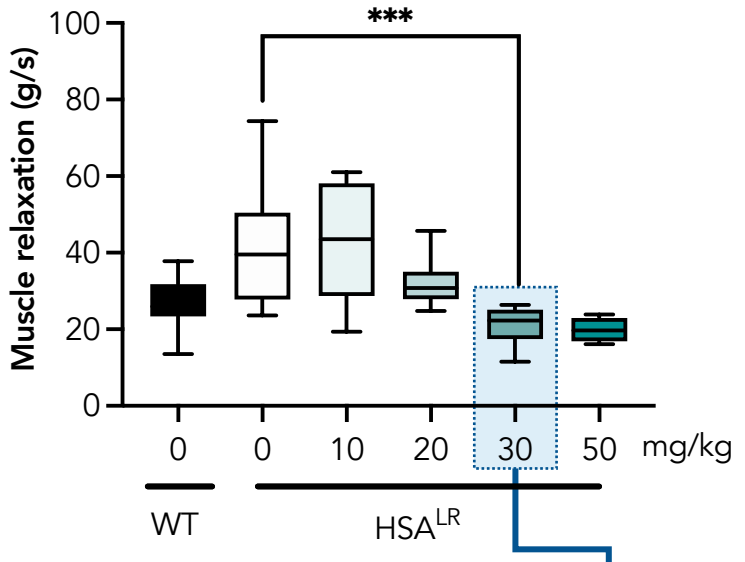


Clcn1



REVERSAL OF MYOTONIA

Rate of muscle relaxation



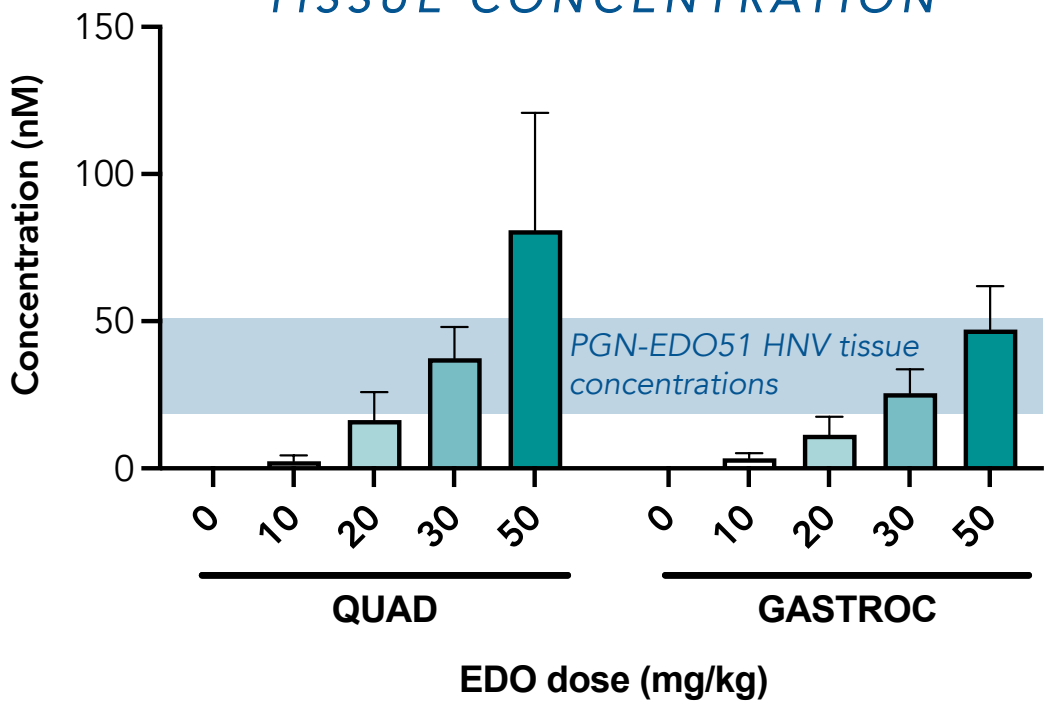
Correction of myotonia observed after a **single dose of 30 mg/kg**

Protocol: PGN-EDODM1 was administered IV to HSA^{LR} mice at doses (mg/kg): 10, 20, 30 (n=8), 50 (n=4) against a saline control (n=16) and wild-type (WT) saline control (n=8). Myotonia assessed, tissues harvested 2 weeks post-administration. Mis-splicing data is quadriceps. Mean ± SEM or min to max. **** = p≤0.0001; *** = p≤0.001.

HUMAN PGN-EDO51 TISSUE CONCENTRATIONS WERE COMPARABLE TO THOSE ACHIEVED IN HSA^{LR} MOUSE MODEL

HSA^{LR} MOUSE

Robust mis-splicing correction and reversal of myotonia were observed after a **single dose of 30 mg/kg**



PGN-EDO51 Ph1

Following a single 10 or 15 mg/kg dose of PGN-EDO51 in our Ph1 HNV trial, **tissue concentrations were similar** to those measured for PGN-EDODM1 at 30 mg/kg

We believe that PGN-EDODM1 has the potential to achieve concentrations in DM1 patients that could lead to **clinically-meaningful outcomes**, supporting further development of this candidate

Protocol: PGN-EDODM1 was administered IV to HSA^{LR} mice at doses (mg/kg): 10, 20, 30 (n=8), 50 (n=4) against a wild-type (WT) saline control (n=8). Tissue concentration assessed by HPLC.

PEPGEN IS ON TRACK TO INITIATE A DM1 PATIENT CLINICAL TRIAL IN 1H23

	2022	2023	2024
Anticipated milestones	• **2Q:** NHP dose range-finding study ✓ • **2H: IND-enabling studies**	• **1H: Initiation of Ph1/2 DM1 patient clinical trial**	• Safety and **splicing data** in DM1 patients (Ph1/2)
Overview	• We believe oligonucleotide tissue concentration readouts from PGN-EDO51 Ph1 study support clinical potential of PGN-EDODM1	• Aim of clinical trials is to assess safety, tolerability and efficacy of PGN-EDODM1 in DM1 patients	

CONCLUSION

James McArthur, Ph.D.

Chief Executive Officer

SCALABLE EDO TECHNOLOGY DESIGNED TO ENABLE BROAD PORTFOLIO

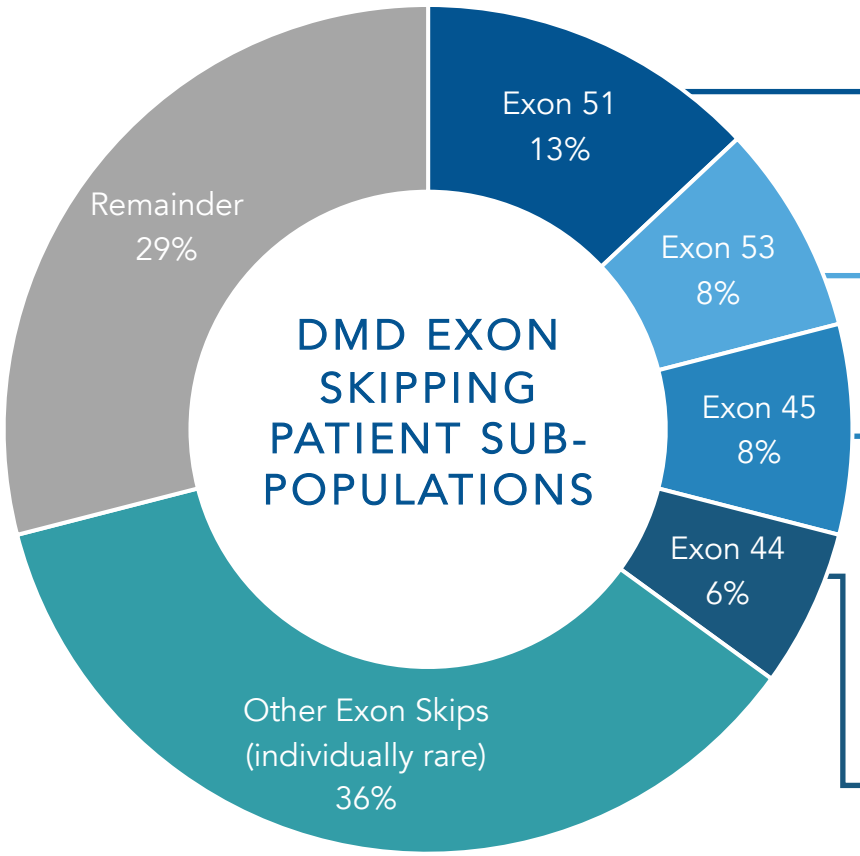
PROGRAM	INDICATION *TARGET*	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT ANTICIPATED MILESTONE
PGN-EDO51	Duchenne muscular dystrophy *Exon 51*						**1H23** *Ph2a patient clinical trial initiation*
PGN-EDODM1	Myotonic dystrophy type 1 *DMPK*						**1H23** *Ph1/2 patient clinical trial initiation*
PGN-EDO53	Duchenne muscular dystrophy *Exon 53*						**2H22** *NHP exon skipping data*
PGN-EDO45	Duchenne muscular dystrophy *Exon 45*						**2H22** *Candidate nomination*
PGN-EDO44	Duchenne muscular dystrophy *Exon 44*						**2H22** *Candidate nomination*

FUTURE PIPELINE OPPORTUNITIES

Additional neuromuscular indications

Neurologic indications

WE ARE COMMITTED TO SERVING THE DMD COMMUNITY



PepGen's clinical program

Exon 51: PGN-EDO51

Next anticipated milestone: Ph2a patient trial initiation (1H23)

PepGen's discovery programs

Exon 53: PGN-EDO53

Next anticipated milestone: NHP exon skipping data (2H22)

Exon 45: PGN-EDO45

Next anticipated milestone: Candidate nomination (2H22)

Exon 44: PGN-EDO44

Next anticipated milestone: Candidate nomination (2H22)

Source: https://www.cureduchenne.org/cure/exon-skipping/.

THE FUTURE OF PEPGEN

2022

PGN-EDO51 (DMD exon 51) Ph1 HNV trial showed:

- **Highest level of single-dose exon skipping and oligo delivery observed in a clinical trial***
- PGN-EDO51 was generally well-tolerated

2023

Anticipate **initiation of patient clinical trials** for DMD & DM1

2024

Anticipate **clinical POC in two indications:**

- Patient dystrophin data (DMD)
- Patient splicing data (DM1)

- 5 neuromuscular disease therapies in pipeline
- Work underway to **leverage EDO platform** to expand to new tissues & new indications

PepGen

* Comparative statements are based on cross-trial comparisons with publicly-available data for other exon skipping approaches that have been assessed following a single dose.

Q&A

THANK YOU