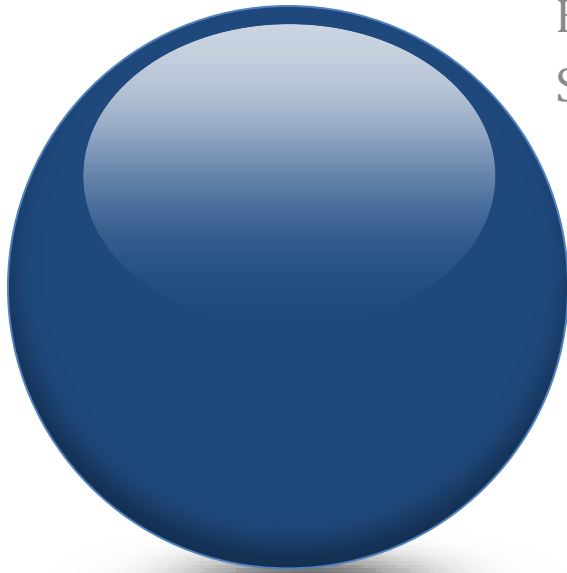


Overview of Clinical Development Programs For Duchenne Muscular Dystrophy

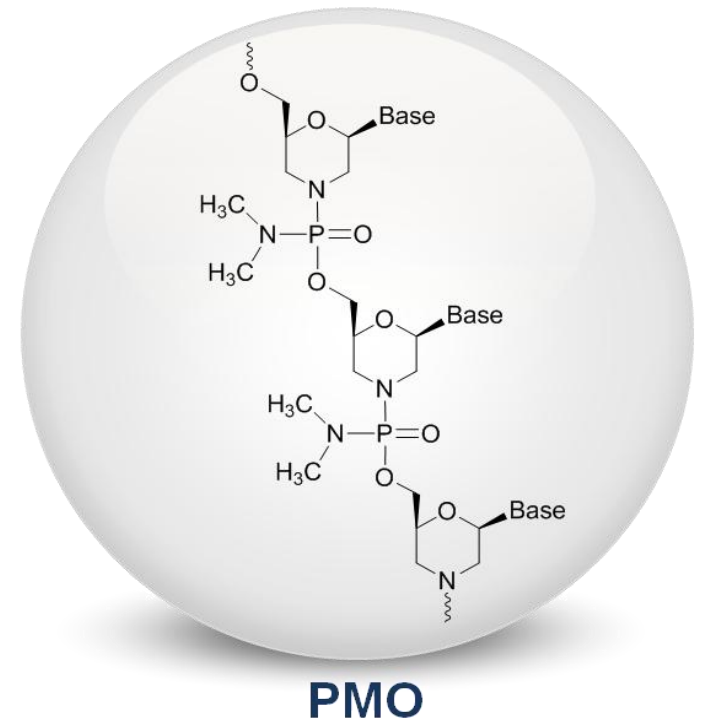
20011-2012

Edward M. Kaye MD
SVP, Chief Medical Officer



Favorable Characteristics of PMO

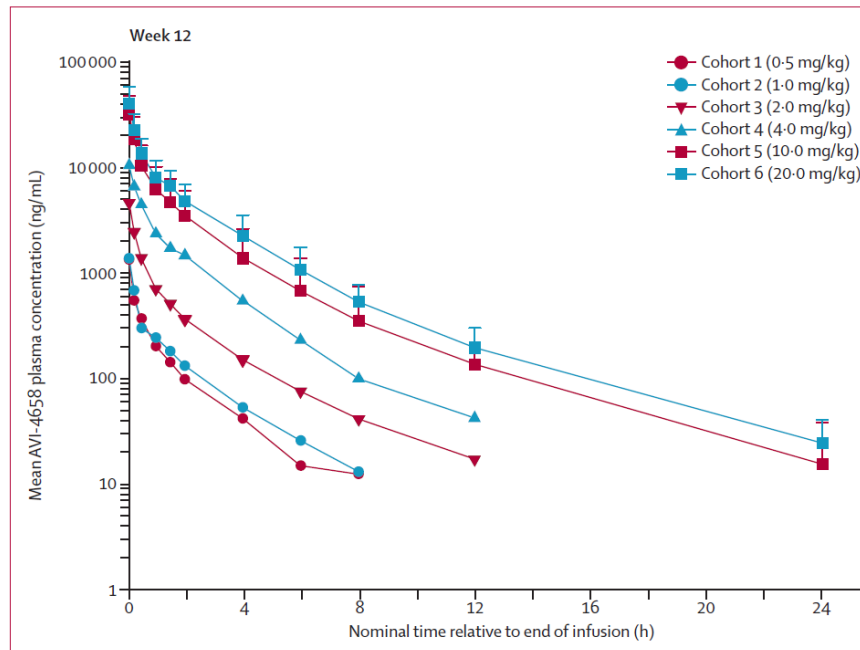
- Tolerated to Maximum Feasible Dose
- No Evidence (Clinical or Preclinical) of:
 - Injection Site Reactions
 - Complement Activation
 - Coagulopathy
 - Innate Immune System Activation
- Act as Steric Blockers:
 - No RNase H Activation
 - No RISC incorporation



Lessons Learned From The Phase 1/2 Trial (Study 28) and Pre-Clinical Data

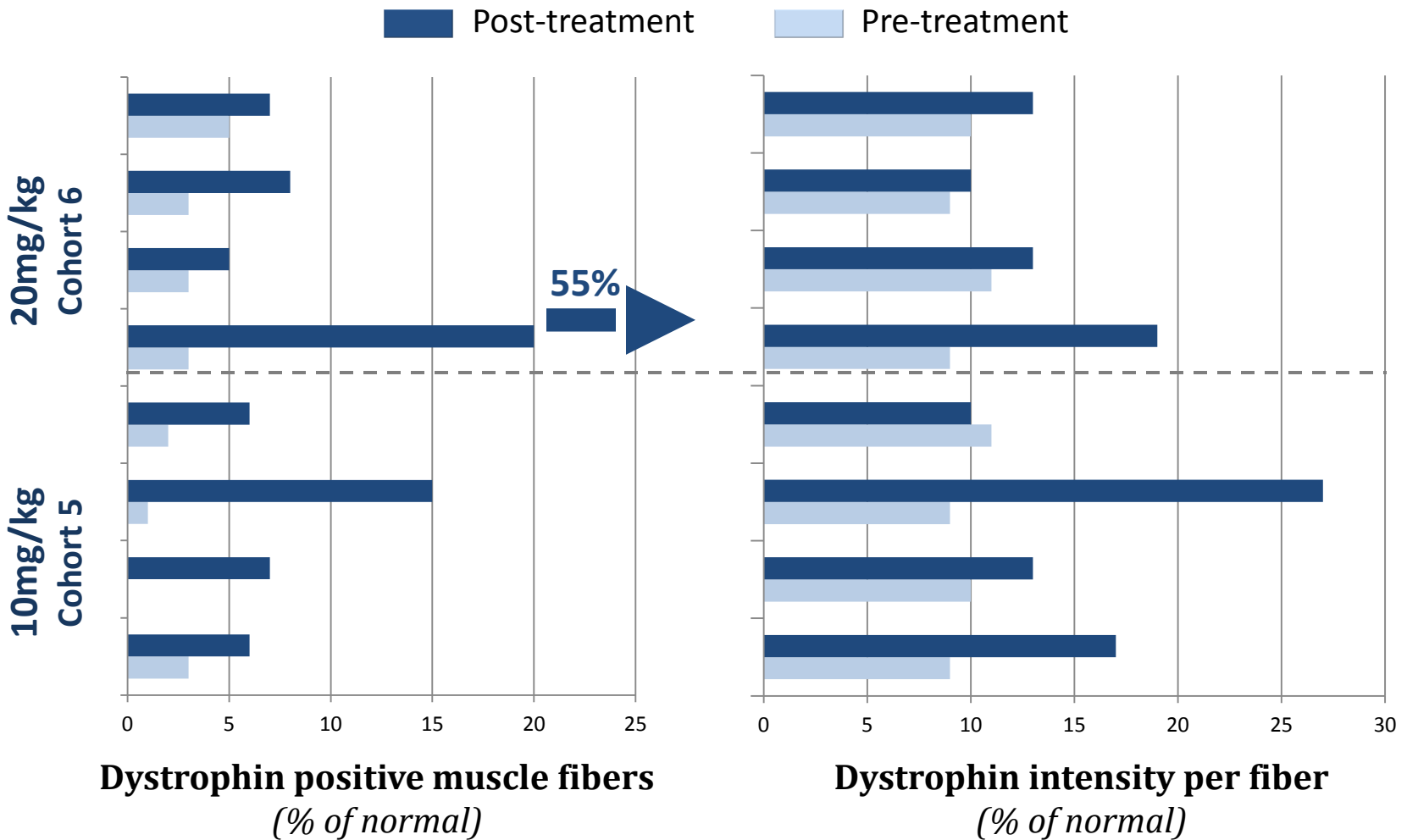
- Dosing appears to be based on a per kilogram basis rather than surface area even in non-human primates
- Eteplirsen is excreted unchanged in the kidney
- Eteplirsen exhibits linear kinetics
- Dose and duration of exposure to Eteplirsen is probably very important to produce effective exon skipping
- Long term data for safety and efficacy is critical
- Safety profile appears very good

Eteplirsen Pharmacokinetics in DMD Patients



Dose (mg/kg)	C _{max} (ng/mL)	AUC _{0-inf} (ng·hr/mL)	AUC _{0-inf} fold AUC _{0-inf} in monkey at 320 mg/kg
0.5	1360 (42)	1568 (129)	1000
1	1339 (549)	1744 (537)	900
2	4823 (804)	6219 (555)	250
4	9500 (4292)	18617 (6920)	80
10	29417 (14338)	39806 (20990)	40
20	38983 (16875)	57271 (24528)	26
30*	57,000	82,000	20
50*	86,000	120,000	13

Eteplirsen: Dose and Duration Important For Dystrophin Expression



Sub-therapeutic cohorts (1-4) not shown.

Eteplirsen Study 28: TEAEs (>1 Event)

Adverse Event	Number	(%)
URTI	8	42
Headache	8	42
Rhinitis	7	37
Back pain	7	37
Fall	5	26
Myalgia	4	21
Tachycardia	3	16
Abdominal pain	3	16
Nausea	3	16
Vomiting	3	16
Influenza like illness	3	16
Arthralgia	3	16
Dizziness	3	16
Upper abdominal pain	2	11
Disease progression	2	11
Fatigue	2	11
Vessel puncture site bruise	2	11
Bronchitis	2	11
Viral infection	2	11
Lumbar vertebral fracture	2	11
Procedural pain	2	11
Pain in extremity	2	11
Cough	2	11
Haematoma	2	11

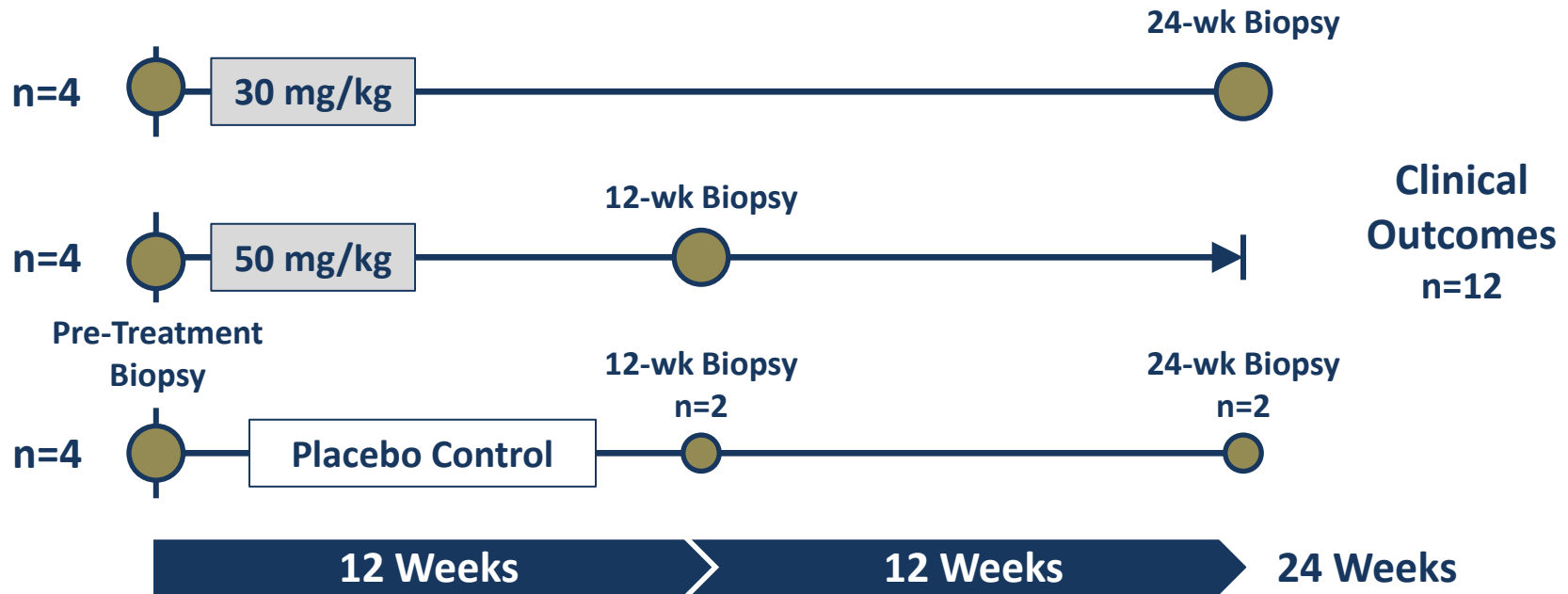
Two SAEs reported:

- Both unrelated to drug: one post-operative nausea and vomiting; one ankle fracture both in 14 week follow-up

One patient withdrawn from Rx:

- Detection of asymptomatic deteriorating cardiomyopathy* after 7 weeks of Rx (elevated troponin). Sinus tachycardia noted on dosing visits from first dose onward. Cardiomyopathy noted in ~6m before study.
- Three other patients reported cardiomyopathy at baseline; four other patients recorded high troponin during study and one at baseline

Eteplirsen Phase II Study Design: Fully Enrolled, Dosing Initiated



● Multiple Endpoints, Collected Frequently:

- Biochemical Markers: Dystrophin and Immune-Inflammatory Response
- Clinical Outcomes: Various Tests of Muscle Function, Strength, and Endurance
- Cardiac and Pulmonary Function Tests
- Safety Monitoring

DMD Phase 2 Program

- Eteplirsen Phase 2 Program Status
 - All 12 patients enrolled
 - All 12 patients dosed
- One US site
- DSMB to be established
- Full results available in Q2 2012
 - blinded biopsy safety data and dystrophin in Q1 following DSMB review

Phase 2 Study Extension

- Phase 2 study extension is being developed as separate protocol
 - Duration planned until approval if warranted by results
 - Clinical end points will be collected at primary site q 3 months
 - Weekly dosing at local site
 - Dosing to single arm or two arms depending on efficacy
 - Contract negotiations with major pharmaceutical manufacturers to ensure adequate long term drug supply almost completed

Phase 3 Eteplirsen Study

- Site selection feasibility to start in Q1 2012
- Estimated 25 sites needed
- Global site locations
- Endpoint selection to be based on Phase 2 data
- Powering of study will depend on Phase 2 data
- EU and Japanese regulatory strategy being developed

Eteplirsen US, EU, and Japan Regulatory Strategy

- US
 - End of Phase II meeting with FDA
- EU
 - Meeting with individual countries for scientific advise
 - Schedule scientific advise meeting with CHMP
 - Begin Pediatric Investigational Plan discussions with PEDCO
- Japan
 - Use Japanese regulatory consultant
 - Include Japanese site in Phase 3 study

Pan Exon Strategy

- Focus on safety of PMO platform with no backbone specific toxicity and sequence specificity without off-target toxicity
- Stress the rarity of exon amenable therapy in general and extreme rarity after the first 5 exons are developed
- Build on the safety and efficacy experience of Exon 51
- Collaborations and Funding sources:
 - Collaboration with Dr. Eric Hoffman's group for Exon 45 development (DOD Funding)
 - NIH TRND grant for Exon 50 (AVI 4038) under contract negotiations
 - EU Innovative Medicines Initiative with Dr. Francesco Muntoni for Exon 53
 - Possible other funding sources for rarer exon development using multi-exon skipping trial