Pfizer PF-06939926: Gene therapy safety and tolerability study in Duchenne muscular dystrophy (DMD)

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Gene Therapy Panel
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Disclaimer

• This presentation includes forward-looking statements about, among other things, development of Pfizer’s Rare Disease products and product candidates, including mini-dystrophin gene therapy (PF-06939926), and its potential benefits, that are subject to substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Additional information regarding these factors can be found in Pfizer’s Annual Report on Form 10-K for the fiscal year ended December 31, 2017 and in our subsequent reports on Form 10-Q, including in the sections thereof captioned “Risk Factors” and “Forward-Looking Information and Factors that May Affect Future Results”, as well as in our subsequent reports on Form 8-K, all of which are filed with the US Securities and Exchange Commission (SEC) and available at www.sec.gov and www.pfizer.com.

• The forward-looking statements in this presentation speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements.
**PF-06939926 (formerly BMB-D001): Background and Rationale**

- Mini-dystrophin sequence selection based on a mild Becker muscular dystrophy patient’s gene sequence.
- Adeno-associated virus, serotype 9 (AAV9) capsid selection based on attributes of virus and serotype.
  - Adeno-associated viruses (AAV) are non-pathogenic
  - AAV9 target tissue= skeletal and cardiac muscles
- Muscle-specific promoter

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**Mini-dystrophin gene sequence selected**

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http://www.genetherapynet.com/viral-vector/adeno-associated-viruses.html;
PF-06939926: DMD\textsuperscript{mdx} Rat Dose-Finding Study

Plasma Biomarker (CK)

TOTAL CREATINE KINASE - 3 months p.i.

- WT + Buffer (n=5)
- DMD + Buffer (n=6)
- DMD + 1E+13 vg/kg (n=6)
- DMD + 3E+13 vg/kg (n=6)
- DMD + 1E+14 vg/kg (n=7)
- DMD + 3E+14 vg/kg (n=5)

TOTAL CREATINE KINASE - 6 months p.i.

- WT + Buffer (n=7)
- DMD + Buffer (n=4)
- DMD + 1E+13 vg/kg (n=6)
- DMD + 3E+13 vg/kg (n=5)
- DMD + 1E+14 vg/kg (n=6)
- DMD + 3E+14 vg/kg (n=5)

C. Le Guiner, World Muscle Society, 2017

Repeated Grip Strength

A 1E+13

B 3E+13

C 1E+14

D 3E+14

- WT (n=9)
- DMD\textsuperscript{mdx} (n=8)
- DMD\textsuperscript{mdx} AAV9 - 1E+13 (n=6)
- DMD\textsuperscript{mdx} AAV9 - 3E+13 (n=9)
- DMD\textsuperscript{mdx} AAV9 - 1E+14 (n=8)
- DMD\textsuperscript{mdx} AAV9 - 3E+14 (n=5)
*Participants: 5-12 year old boys with DMD:
  - Ambulant and on daily glucocorticoids
  - AAV9 NAb (-)

*Single intravenous (IV) infusion

*Staggered dosing for both cohorts
  - 6 weeks between subjects 1-2;
  - 3 weeks between subjects 2-6

*Primary endpoint: Safety through 12 months

*Other endpoints:
  - Dystrophin expression and transduction
  - Long-term safety (through 5 years)

*External Data Monitoring Committee (E-DMC) data review prior to advancing to Cohort 2.
PF-06939926: Current Phase 1b DMD Safety Gene Therapy Study Status (NCT03362502)

- Sites activated in US: 3
- Recruitment:
  - Screened: 4
    - Screen failure: 1 (ambulatory criterion)
  - Enrolled: 3
  - Dosed: 3

![](chart.png)

# Months from PF-06939926 IV infusion
PFIZER AIMS TO BECOME INDUSTRY LEADER IN GENE THERAPY WITH ACQUISITION OF BAMBOO THERAPEUTICS, INC.
Monday, August 1, 2016, 10:00 AM EDT

Bamboo’s portfolio includes potential best-in-class rAAV-based gene therapies that will complement Pfizer’s rare disease and gene therapy portfolios in two priority areas: neuromuscular, with a pre-clinical asset for Duchenne Muscular Dystrophy (DMD); …. 

Bamboo’s approximately 11,000-square foot, fully staffed and operational manufacturing facility has experience producing Phase I/II materials using a superior suspension, cell-based production platform that increases scalability, efficiency and purity. This helps enable the DMD program and other projects requiring large amounts of rAAV. The facility, previously known as the University of North Carolina Vector Core facility, has served as a qualified supplier of rAAV vectors for several healthcare companies and academic institutions.

PFIZER BOOSTS NORTH CAROLINA FOOTPRINT WITH $100 MILLION EXPANSION
Barry Teater, NCBiotech
Monday, August 7, 2017, 12:00 AM EST

Pfizer, the global pharmaceutical giant, will expand its vaccine-manufacturing plant in Sanford with a $100 million investment in gene therapy manufacturing that will add 40 jobs to its workforce… The expansion is the latest of several recent decisions by Pfizer to expand its footprint in North Carolina and to build an industry leading, end-to-end, global gene therapy business.
Design features influenced by advocacy organizations:

- Informed consent process
- Participant selection
- Travel support
- Steroid management
- Biopsy collection, handling, and follow-up care
- Activity monitoring
- External data monitoring committee membership
- Communications
- Data sharing

Thanks for keeping us informed of what matters to patients!
PFIZER THANKS ALL ADVOCACY, INVESTIGATIVE SITES, AND FAMILIES!!!
PF-06939926 dose-dependent increase in mini-dystrophin positive fibers correlates with dose-dependent decrease in fibrosis.

NOTE: Letters above error bars in graphs: bars not sharing the same letter are significantly different (ANOVA analysis + Fisher’s post-hoc bilateral test).