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Marathon Pharmaceuticals Presents Analyses at AAN of a Phase III Clinical Study of Deflazacort in Patients with Duchenne Muscular Dystrophy (DMD)

Investigational Drug Deflazacort Has Fast Track Status, Orphan Drug Designation and Rare Pediatric Disease Designation for DMD from FDA

Vancouver, Canada, April 19 – Marathon Pharmaceuticals, a biopharmaceutical company focused solely on finding treatments for rare diseases, today announced presentations of analyses of a pivotal Phase III study of deflazacort, an investigational glucocorticoid, in patients with Duchenne Muscular Dystrophy (DMD). Results are being shared at the 68th American Academy of Neurology (AAN) Annual Meeting in Vancouver, Canada.

The AAN presentations provide further detail on the previously presented primary endpoint of the pivotal study, which showed deflazacort improved muscle strength in DMD patients versus placebo at 12 weeks ($p=0.0173$ and $p=0.0003$ for 0.9 mg/kg/d and 1.2 mg/kg/d doses, respectively). Results of timed functional tests (TFT), a secondary endpoint being presented at AAN, show deflazacort patients at both doses had significant improvement from baseline to Week 12 versus placebo in the ability to perform three tests: time from lying down to standing, time to climb four stairs, and time to run or walk 30 feet ($p<0.002$). The most common adverse events were cushingoid appearance, hirsutism, weight gain, central obesity and increased appetite.¹

In addition, Marathon is presenting post-hoc analyses showing the effects of deflazacort on muscle strength and pulmonary function in the subset of DMD patients who had lost the ability to walk. The most common adverse events in the deflazacort treatment arms for the post-hoc analyses of non-ambulatory patients were cushingoid appearance, erythema, central obesity, weight gain and headache.^{2,3}

“DMD is a severe disease that quickly progresses without treatment, there is a great need for approved therapies that improve symptoms for patients in all stages of the disease, said Jordan Dubow, MD, Chief Medical Officer, Marathon Pharmaceuticals. “These data provide important detail on the potential benefit deflazacort may have in treating DMD patients, regardless of their mobility and disease severity.”

There is no cure for DMD, and currently no FDA approved treatment. The FDA has granted Fast Track status, Orphan Drug designation and Rare Pediatric Disease designation for deflazacort for DMD. Marathon expects to submit a New Drug Application for deflazacort in May 2016 and, if approved by FDA, deflazacort could be made commercially available in the U.S. in early 2017.

DMD is the most common and most severe form of muscular dystrophy, and affects mainly boys and young men.⁴ The disease is marked by progressive muscle weakening and wasting, leading ultimately to the inability to walk by the teen years or earlier and severe respiratory and cardiac complications.^{5,6} Few patients live into their thirties.⁶

Prior to FDA evaluation, Marathon is making deflazacort available to qualified patients, at no cost, through ACCESS DMD™, an Expanded Access Program operating under FDA authorization. Patients, families and physicians can learn more about ACCESS DMD™, including a list of clinical sites participating in the program, by visiting <http://www.AccessDMD.com> or calling 1-844-800-4DMD (4363).

“As a physician who works with dozens of boys and young men with DMD, every day I see the impact this serious disease has on the patients and the families that care for them,” said Nancy Kuntz, MD, Attending Physician, Division of Neurology and Medical Director, Muscular Dystrophy Association Clinics at the Ann & Robert H. Lurie Children’s Hospital in Chicago, Illinois. “There is a critical need for FDA-approved treatments for DMD patients, and this expanded access program offers hope while the deflazacort regulatory submission is pending.”

About the analyses presented at AAN

The pivotal Phase III trial was a randomized, double-blind, placebo controlled and active comparator study in 196 patients with DMD. Patients were randomized to either deflazacort 0.9 mg/kg/day, deflazacort 1.2 mg/kg/day, prednisone 0.75 mg/kg/day or placebo for 12 weeks. The primary endpoint was change in average muscle strength from baseline to Week 12 with deflazacort and prednisone compared to placebo measured by the Medical Research Council Index (MRC). Deflazacort met the primary endpoint at Week 12 vs placebo ($p=0.0173$ and $p=0.0003$ for 0.9 mg/kg/d and 1.2 mg/kg/d doses, respectively vs. -0.10 for placebo). After 12 weeks, placebo patients were re-randomized to either of the three active treatments from weeks 12 – 52 and those not randomized to placebo were maintained on their blinded active treatment through 52 weeks. Muscle strength and timed functional tests, were included in the analysis.¹

The analyses of non-ambulatory patients were post-hoc and not pre-specified. Muscle strength in non-ambulatory DMD patients, deflazacort at 0.9 mg/kg/d and 1.2 mg/kg/d were assessed, with the deflazacort 1.2mg/kg/d arm reaching statistical significance at Week 12 versus placebo ($p=0.04$).²

Pulmonary function tests with the same subset of patients over 12 weeks, patients receiving 0.9 mg/kg/d and 1.2 mg/kg/d doses of deflazacort were also assessed, including forced vital capacity (FVC) and maximum voluntary ventilation (MVV). Some measures showed or trended toward statistical significance.³

Marathon is presenting additional deflazacort analyses and other data as posters at AAN, including:

- Effects of Deflazacort on Growth and Development in Juvenile Rats
- Effect of Deflazacort and Prednisone on Muscle Enzymes in the Treatment of Duchenne Muscular Dystrophy
- Potential Mechanisms for Prolonged Loss of Ambulation with Deflazacort in Duchenne Muscular Dystrophy: Tolerability Profile and Effects on Growth

About deflazacort

Deflazacort is a glucocorticoid with anti-inflammatory and immunosuppressant properties.⁷ Based on published clinical studies, it appears that deflazacort may be an

important new treatment option for patients with DMD.^{8,9} Side effects reported to date include cushingoid appearance, hirsutism, weight gain, erythema, nasopharyngitis, irritability and cataract formation.¹

Deflazacort is an investigational drug not currently approved in the U.S. It is available in some countries outside the U.S., where it is approved for a number of uses, but not for DMD.

About Marathon Pharmaceuticals

Marathon Pharmaceuticals, LLC, is a biopharmaceutical company that develops treatments for rare diseases, with a focus on patients who currently have no treatment options. The company's pipeline of new medicines includes treatments for rare neurological and movement disorders. Marathon is headquartered in Northbrook, Illinois, with offices in Chicago, New Jersey and Washington D.C. For more information, visit www.marathonpharma.com.

Media contacts

Greg Aronin
Marathon Pharmaceuticals
(847)-715-0700
info@marathonpharma.com

Christy Maginn
Burson Marsteller
(646) 280-5210
Christy.Maginn@bm.com

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