



PTC Therapeutics Announces FDA Approval of Evrysdi™ (risdiplam) for the Treatment of Spinal Muscular Atrophy in Adults and Children 2 Months and Older

August 7, 2020

- Evrysdi represents the first at home, oral treatment approved for infants, children and adults with all SMA types-

- Marketing Authorization Application submission to European Medicines Agency is imminent -

- Risdiplam is the first approved therapy discovered and developed from PTC Therapeutics' proprietary splicing platform

SOUTH PLAINFIELD, N.J., Aug. 7, 2020 /PRNewswire/ -- PTC Therapeutics, Inc. (NASDAQ: PTCT) today announced that the U.S. Food and Drug Administration (FDA) has approved Evrysdi™ (risdiplam), the first at-home, orally administered treatment for spinal muscular atrophy (SMA) in adults and children 2 months and older. Evrysdi showed clinically meaningful improvements in motor function and attainment of developmental milestones across two trials in patients age two months and above and across all levels of disease severity, including types 1, 2, and 3 SMA. Infants achieved key motor milestones not normally seen in the natural course of the disease, such as the ability to sit without support. Evrysdi also preserved vital functions and improved survival at 12 months. In particular, Evrysdi improved survival without permanent ventilation compared to natural history when measured at 12 and 23 months.

"Today marks an incredibly important moment for the broader SMA patient community that had been in dire need of safe and effective treatment options," said Stuart W. Peltz, Ph.D., Chief Executive Officer, PTC Therapeutics. "We are appreciative of the patients, physicians and others involved with its development, and our partners at the SMA Foundation and Roche. We are proud that the first oral treatment for spinal muscular atrophy patients was discovered through our splicing platform. I believe that this is one of the most innovative products in the pharmaceutical industry and we are gratified to have played a key role in its discovery and development."

Evrysdi has been studied in a robust clinical trial program in SMA with more than 450 patients and subjects. The program includes infants aged 2 months to adults aged 60 with a range of symptoms and motor function including patients with scoliosis or joint contractures. Patients previously treated for SMA with other medications were also included. The approval is based on results from two clinical studies designed to represent a broad spectrum of patients living with SMA: FIREFISH in symptomatic infants aged 2 to 7 months; and SUNFISH, in children and adults aged 2 to 25 years. SUNFISH is the first and only placebo-controlled trial to include adults with types 2 and 3 SMA.

"We started looking for treatments for SMA more than a decade ago," said Loren Eng, President of the SMA Foundation. "PTC was one of the companies that embraced and remained committed to the idea of developing a truly innovative therapeutic for this disease. We are proud to be part of the collaboration that brought the first oral SMA treatment for patients."

In FIREFISH, 41% (7/17) of infants treated with the therapeutic dose achieved the ability to sit without support for at least 5 seconds as measured by the Bayley Scales of Infant and Toddler Development Third Edition (BSID-III). Additionally, 90% (19/21) of infants were alive without permanent ventilation at 12 months of treatment and reached 15 months of age or older. As described in the natural history of untreated infantile-onset SMA, infants would not be expected to be able to sit independently and only 25 percent of infants would be expected to survive without permanent ventilation beyond 14 months of age. In SUNFISH, children and adults treated with Evrysdi experienced a statistically significant and clinically meaningful improvement in motor function at 12 months (1.55 point mean difference; $p = 0.0156$) compared to placebo, as measured by a change in baseline on the Motor Function Measure-32 (MFM-32) scale.

Evrysdi demonstrated a favorable efficacy and safety profile, with the safety profile established across the FIREFISH and SUNFISH trials. The most common adverse reactions were fever, diarrhea, and rash in later-onset SMA. In infantile-onset SMA, the most common adverse events were similar and also included upper respiratory tract infection, pneumonia, constipation, and vomiting. There were no treatment-related safety findings leading to withdrawal from any study. Ophthalmological monitoring is not required.

Evrysdi will be available in the United States within two weeks for direct delivery to patients' homes through Accredo Health Group Inc., an Express Scripts specialty pharmacy.

Evrysdi will be marketed in the United States by Genentech, a member of the Roche Group, and received an orphan drug designation from FDA in 2017. Outside the United States, Roche holds global commercialization rights to risdiplam, and the European Medicines Agency (EMA) previously granted PRIME (Priority Medicines) designation to risdiplam in 2018 for the treatment of people with SMA and an orphan drug designation in 2019. The submission of a marketing authorization application (MAA) to EMA for risdiplam is pending. At this time, Roche has submitted applications for approval in Brazil, Chile, China, Indonesia, Russia, South Korea and Taiwan.

Evrysdi is a product of the SMA collaboration between PTC, the SMA Foundation, and Roche.

About Evrysdi™ (risdiplam)

Evrysdi is a survival motor neuron 2 (SMN2)-directed RNA splicing modifier designed to treat SMA caused by mutations in chromosome 5q that lead to SMN protein deficiency. Evrysdi is designed to distribute evenly to all parts of the body, including the central nervous system (CNS). Evrysdi is administered daily at home in liquid form by mouth or feeding tube.

About the Clinical Studies

FIREFISH (NCT02913482)

FIREFISH, an open-label, two-part pivotal study, was designed to assess Evrysdi safety, tolerability, efficacy, pharmacokinetics (PK) and pharmacodynamics (PD) in patients aged 1 to 7 months with Type 1 SMA. Part 1 evaluated several doses of Evrysdi and determined the therapeutic dose of 0.2 mg/kg for Part 2. In Part 1, after 12 months of Evrysdi treatment:

- 41% (7/17) of infants treated with the therapeutic dose achieved the ability to sit without support for at least 5 seconds as measured by the BSID-III gross motor scale.
- 90% (19/21) of all infants were alive without permanent ventilation* and reached 15 months of age or older.
- 81% (17/21) of all patients were alive without permanent ventilation* after a minimum of 23 months of treatment and reached an age of 28 months or older (median 32 months; range 28-45 months)

*Permanent ventilation defined as tracheostomy or ≥ 16 hours of non-invasive ventilation per day or intubation for ≥ 21 consecutive days in the absence of, or following the resolution of, an acute reversible event.

SUNFISH (NCT02908685)

SUNFISH, a two-part, placebo-controlled, multicenter pivotal trial, was designed to assess Evrysdi safety, tolerability, efficacy, PK and PD in people with type 2 or 3 SMA aged 2 to 25, including those with scoliosis (67% in Part 2) and joint contractures at baseline. In Part 2, after 12 months, Evrysdi treatment led to:

- A clinically meaningful and statistically significant improvement in motor function among children and adults, as measured by a change in baseline in the MFM-32 total score (1.55 point mean difference; $p = 0.0156$), at 12 months as compared to placebo (1.36 points [risdiplam treatment arm -95% CI: 0.61, 2.11]; [placebo treatment arm: -0.19 points 95% CI: 1.22, 0.84]). MFM-32 assesses 32 different motor functions across a wide range of people with SMA.
- Improved upper limb motor function compared to baseline, as measured by the Revised Upper Limb Module (RULM), a secondary independent motor function endpoint of the study (1.59 point difference; $p=0.0028$).

Clinical Trial Safety Data

The safety profile of Evrysdi was established across FIREFISH and SUNFISH pivotal trials. The most common adverse reactions in later-onset SMA (incidence of at least 10% of patients treated with Evrysdi and more frequently than control) were fever, diarrhea, and rash. The most common adverse reactions in infantile-onset SMA were similar to those observed in later-onset SMA patients. Additionally, the most common adverse reactions (incidence of at least 10%) were upper respiratory tract infection, pneumonia, constipation, and vomiting.

About the Evrysdi Clinical Trial Program

In addition to FIREFISH and SUNFISH, Evrysdi is being evaluated in a broad range of people with SMA, including in:

- JEWELFISH (NCT03032172): an open-label exploratory trial designed to assess the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) in people with SMA aged 6 months to 60 years who received other investigational or approved SMA therapies for at least 90 days prior to receiving Evrysdi. Recruitment for this study is complete with 174 people enrolled.
- RAINBOWFISH (NCT03779334): an open-label, single-arm, multicenter study investigating the efficacy, safety, pharmacokinetics and pharmacodynamics of Evrysdi in infants (~n=25), from birth to six weeks of age (at first dose) with genetically diagnosed SMA who are not yet presenting with symptoms. The study is currently recruiting.

About Spinal Muscular Atrophy (SMA)

Spinal muscular atrophy (SMA) is a severe, inherited, progressive neuromuscular disease that causes devastating muscle atrophy and disease-related complications. It is the most common genetic cause of infant mortality and one of the most common rare diseases, affecting approximately one in 11,000 babies¹. SMA leads to the progressive loss of nerve cells in the spinal cord that control muscle movement. Depending on the type of SMA, an individual's physical strength and their ability to walk, eat or breathe can be significantly diminished or lost.

SMA is caused by a mutation in the survival motor neuron 1 (SMN1) gene that results in a deficiency of SMN protein. SMN protein is found throughout the body and increasing evidence suggests SMA is a multi-system disorder and the loss of SMN protein may affect many tissues and cells, which can stop the body from functioning.

About PTC Therapeutics, Inc.

PTC is a science-driven, global biopharmaceutical company focused on the discovery, development and commercialization of clinically differentiated medicines that provide benefits to patients with rare disorders. PTC's ability to globally commercialize products is the foundation that drives investment in a robust and diversified pipeline of transformative medicines and our mission to provide access to best-in-class treatments for patients who have an unmet medical need. To learn more about PTC, please visit us at www.ptcbio.com and follow us on Facebook, on Twitter at @PTCBio, and on LinkedIn.

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Forward-Looking Statements:

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. All statements contained in this release, other than statements of historical fact, are forward-looking statements, including statements regarding: the future expectations, plans and prospects for PTC; the timing of commercial availability and potential methods of distribution for Evrysdi; advancement of PTC's joint collaboration program in SMA, including any potential regulatory submissions, regulatory approvals or commercial prospects; PTC's strategy, future operations, future financial position, future revenues and, projected costs; and the objectives of management. Other forward-looking statements may be identified by the words "guidance", "plan," "anticipate," "believe," "estimate," "expect," "intend," "may," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions.

PTC's actual results, performance or achievements could differ materially from those expressed or implied by forward-looking statements it makes as a result of a variety of risks and uncertainties, including those related to: the outcome of pricing, coverage and reimbursement negotiations with third party payors for PTC's products or product candidates that PTC commercializes or may commercialize in the future, including Evrysdi; the enrollment, conduct, and results of studies under the SMA collaboration and events during, or as a result of, the studies that could delay or prevent further development under the program, including any potential regulatory submissions and potential commercialization with regards to Evrysdi; the eligible patient base and commercial potential of Evrysdi or any of PTC's other product candidates; and the factors discussed in the "Risk Factors" section of PTC's most recent Quarterly Report on Form 10-Q and Annual Report on Form 10-K, as well as any updates to these risk factors filed from time to time in PTC's other filings with the SEC. You are urged to carefully consider all such factors.

As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. There are no guarantees that any product or product candidate will receive or maintain regulatory approval in any territory, or prove to be commercially successful, including Evrysdi.

The forward-looking statements contained herein represent PTC's views only as of the date of this press release and PTC does not undertake or plan to update or revise any such forward-looking statements to reflect actual results or changes in plans, prospects, assumptions, estimates or projections, or other circumstances occurring after the date of this press release except as required by law.

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