Confirmatory Part 2 of FIREFISH Demonstrates Survival and Motor Milestones Not Seen in Natural History in Infants with Type 1 Spinal Muscular Atrophy

April 28, 2020

- Part 2 of pivotal study met its primary endpoint by demonstrating unsupported sitting in infants aged 1-7 months with type 1 SMA after 12 months of treatment -

- Meaningful benefit observed in dose-finding Part 1 confirmed -

- PDUFA expected August 24, 2020 -

SOUTH PLAINFIELD, N.J., April 28, 2020 /PRNewswire/ -- PTC Therapeutics, Inc. (NASDAQ: PTCT) today announced positive results from part 2 of the pivotal FIREFISH study evaluating risdiplam in infants with type 1 spinal muscular atrophy (SMA). The global study met its primary endpoint of infants sitting without support for five seconds by month 12, as assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development Third Edition (BSID-III). Type 1 SMA babies do not achieve this milestone without therapy. Substantial results were demonstrated across multiple secondary and exploratory endpoints, as infants in the study achieved milestones not seen in natural history. In addition to being able to sit without support, infants were able to maintain upright head control, roll to the side, and stand without support after 12 months of treatment. At 12 months, 95% infants maintained the ability to swallow and 89% were able to feed orally. No new safety signals were identified in part 2 of the study. These data will be reviewed during a conference call today at 11:30 am ET by our development partner, Roche.

"The positive results from part 2 of the FIREFISH study reinforce the clinically meaningful efficacy seen in part 1 of the trial and support its overall safety profile," said Stuart W. Peltz, Ph.D., Chief Executive Officer of PTC Therapeutics. "This is even more impressive since this study included many patients whose disease had already progressed significantly before starting treatment. We expect that risdiplam will be the most competitive global product for a broad range of SMA patients and are confident in Roche's ability to conduct a robust launch following approval. A significant unmet need exists within the SMA population, particularly for an oral, at home therapy in the current environment."

The single-arm part 2 of FIREFISH assessed the efficacy of risdiplam in 41 infants (eligible age at enrollment between 1 and 7 months) with type 1 SMA treated for 12 months. The study met its primary endpoint with 29% of infants (12/41; $p<0.0001$) sitting without support for five seconds by month 12, as assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development Third Edition (BSID-III). No infants achieve this milestone in the natural history of type 1 SMA. In addition, 18 (43.9%) infants were able to hold their head upright, 13 (31.7%) were able to roll to the side and 2 (4.9%) infants were able to stand with support, as measured by the Hammersmith Infant Neurological Examination 2 (HINE-2). Safety for risdiplam in the FIREFISH study was consistent with its known safety profile.

After 12 months of treatment with risdiplam 93% (38/41) of infants were alive and 85% (35/41) were event-free. At the time of analysis, the median duration of treatment was 15.2 months and the median age was 20.7 months. Without treatment, the median age of death or permanent ventilation was 13.5 months in a natural history study. Three infants experienced fatal complications of their disease within the first three months of treatment. None of these events have been attributed by the investigator as related to risdiplam. 90% (37/41) had a CHOP-INTEND score increase of at least 4 points, with 56% (23/41) achieving a score above 40; the median increase was 20 points. Without treatment, infants with type 1 SMA show a decrease in CHOP-INTEND scores over time.

In an exploratory endpoint, 95% of infants who were alive at 12 months (36/38) maintained the ability to swallow and 89% (34/38) were able to feed orally. In contrast, in a natural history cohort, all infants with type 1 SMA older than 12 months required feeding support.

Safety for risdiplam in the FIREFISH study was consistent with its previously reported safety profile and no new safety signals were identified. The most common adverse events (AE) were upper respiratory tract infection (46.3%), pneumonia (39%), pyrexia (39%), constipation (19.5%) nasopharyngitis (12.2%), rhinitis (12.2%) and diarrhea (9.8%). The most common serious adverse events were pneumonia (31.7%), bronchiolitis (4.9%), respiratory failure (4.9%) and hypotonia (4.9%).

Risdiplam is being studied in the broadest clinical trial program in SMA, with patients ranging from birth to 60 years old, and includes pre-symptomatic patients and those previously treated with other SMA-targeting therapies. The clinical trial population was designed to represent the broad, real-world spectrum of people living with this disease with the aim of ensuring access for all appropriate patients.

The FDA recently extended the Prescription Drug User Fee Act (PDUFA) date for its review of the New Drug Application (NDA) of risdiplam to August 24, 2020, following the submission of additional data, including comprehensive data from Part 2 of the SUNFISH Trial. The inclusion of these data in the submission could potentially allow for placebo-controlled data on patients 2-25 years of age to be included on the label, and support market access and reimbursement for the broadest range of SMA patients. The SMA program is a collaboration between PTC, the SMA Foundation, and Roche.

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 babies. 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 Risdiplam
Risdiplam is an investigational survival motor neuron 2 (SMN2) splicing modifier for SMA and is an orally administered liquid. It is designed to durably increase and sustain SMN protein levels both throughout the central nervous system and in peripheral tissues of the body. Risdiplam is being studied in a broad clinical trial program in SMA, with patients ranging from birth to 60 years old, and includes patients previously treated with other SMA-targeting therapies. The clinical trial population represents the broad, real-world spectrum of people living with this disease. The risdiplam clinical development program was designed with the aim of enabling access for all appropriate patients.

Risdiplam is currently being evaluated in four multicenter trials in people with SMA:

- FIREFISH (NCT02913482) – an open-label, two-part pivotal clinical trial in infants with type 1 SMA. Part 1 was a dose-escalation study in 21 infants. The primary objective of Part 1 was to assess the safety profile of risdiplam in infants and determine the dose for Part 2. Part 2 is a pivotal, single-arm study of risdiplam in 41 infants with type 1 SMA treated for 24 months, followed by an open-label extension. Enrollment for Part 2 was completed in November 2018. The primary objective of Part 2 is to assess efficacy as measured by the proportion of infants sitting without support after 12 months of treatment, as assessed in the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development – Third Edition (BSID-III) (defined as sitting without support for 5 seconds).
- SUNFISH (NCT02908685) – SUNFISH is a two-part, double-blind, placebo-controlled pivotal study in people aged 2-25 years with types 2 or 3 SMA. Part 1 (n=51) determined the dose for the confirmatory Part 2. Part 2 (n=180) evaluated motor function using total score of Motor Function Measure 32 (MFM-32) at 12 months. MFM-32 is a validated scale used to evaluate fine and gross motor function in people with neurological disorders, including SMA.
- JEWELFISH (NCT03032172) – an open-label exploratory trial in people with SMA aged 6 months–60 years who have been previously treated with SMA-directed therapies (n=174). The study has completed recruitment.
- RAINBOWFISH (NCT03779334) – an open-label, single-arm, multicenter study, investigating the efficacy, safety, pharmacokinetics and pharmacodynamics of risdiplam in babies (~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 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 historic fact, are forward-looking statements, including statements regarding: the future expectations, plans and prospects for PTC; 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, 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 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 risdiplam; the eligible patient base and commercial potential of risdiplam or any of PTC's other product candidates; and the factors discussed in the "Risk Factors" section of PTC's most recent 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 will receive or maintain regulatory approval in any territory, or prove to be commercially successful, including risdiplam.

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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