PTC Therapeutics Announces 2-year Data from Part 1 of SUNFISH and New Data from JEWELFISH Trials for Risdiplam in Patients with Spinal Muscular Atrophy

June 12, 2020

- Risdiplam significantly improved motor function after 24 months of treatment in people aged 2-25 years with type 2 or 3 SMA in SUNFISH Part 1 -

- Preliminary 12-month data in the JEWELFISH study in previously treated patients demonstrated increases in SMN protein levels -

- Data presented at Virtual CureSMA Conference -

SOUTH PLAINFIELD, N.J., June 12, 2020 /PRNewswire/ -- PTC Therapeutics, Inc. (NASDAQ: PTCT) today announced two-year data from Part 1 of the SUNFISH trial in children and adults with type 2 or 3 spinal muscular atrophy (SMA) and new preliminary 12-month data from JEWELFISH. The results of an exploratory efficacy analysis from SUNFISH showed risdiplam significantly improved motor function after 24 months of treatment compared to natural history data (Motor Function Measure Scale (MFM) 3.99 point difference; p< 0.0001). In addition, preliminary 12-month data from the JEWELFISH trial in people with SMA aged 6 months to 60 years, previously treated with other SMA therapies, showed that treatment with risdiplam led to rapid and sustained increases in SMN protein levels. No new safety signals were observed and the overall adverse event profile was consistent with that of treatment-naive patients.

"We continue to be highly encouraged by the positive results observed in the SUNFISH and JEWELFISH trials that further support the long-term benefits of risdiplam," said Stuart W. Peltz, Ph.D., Chief Executive Officer of PTC Therapeutics. "These results are clinically meaningful with a favorable safety profile. They also reinforce the potential of risdiplam as a differentiated, oral therapy to improve motor function for children and adults with SMA. We anticipate that risdiplam will be a new and meaningful at-home treatment for a broad range of people affected by this devastating disease."

The exploratory efficacy analysis of Part 1 of the SUNFISH study assessed motor function, using the Motor Function Measure (MFM) scale, which is used to evaluate fine and gross motor function in people with neurological disorders including SMA. It assesses different motor functions ranging from the use of hands and fingers to standing and walking. In a weighted analysis comparing the data with an external natural history comparator cohort, the MFM total change from baseline at Month 24 was greater in patients receiving risdiplam (3.99 point difference (95% CI: 2.34, 5.65) p< 0.0001). These results are consistent with the results of the pivotal Part 2 of the trial at 12 months in non-ambulatory patients, which demonstrated that change from baseline in total MFM-32 score was significantly greater in people treated with risdiplam, compared to placebo (1.55 point mean difference; p=0.0156). The most common adverse events in Part 1 of the SUNFISH study were fever (pyrexia; 55%), cough (35%), vomiting (33%), upper respiratory tract infections (31%), cold (nasopharyngitis; 24%), and persistent sore throat (oropharyngeal pain; 22%). The most common serious adverse event that occurred in three of the 51 patients exposed to risdiplam was pneumonia. To date there have been no treatment-related safety findings leading to withdrawal.

Enrollment for the JEWELFISH study, assessing safety and pharmacodynamics of risdiplam in previously treated patients with SMA, who are now receiving risdiplam, is complete (n=174). Among the patients who had completed 12 months of treatment with risdiplam (n=18), a rapid and sustained two-fold increase in median SMN protein levels versus baseline was observed. An early assessment of safety showed a consistent safety profile compared to treatment-naive patients.

Of the 174 patients enrolled in the JEWELFISH study, 76 were previously treated with nusinersen and 14 with onasemnogene abeparvovec. The remaining patients had been treated in previous Roche SMA clinical trials.

In the JEWELFISH study, the most common adverse events were upper respiratory tract infections (13%), headache (12%), fever (8%), diarrhea (8%), nasopharyngitis (7%) and nausea (7%). To date there have been no drug-related safety findings leading to withdrawal and the overall adverse event profile has been similar to that observed in risdiplam trials of patients not previously treated with an SMA-targeting therapy.

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.

In November 2019, the U.S Food and Drug Administration granted Priority Review for risdiplam with an expected decision on approval by August 24, 2020. 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 loss of function mutations or deletions of 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.

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 increase and sustain SMN protein levels both throughout the central nervous system and in peripheral tissues of the body. Risdiplam is being studied in the broadest 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 diverse, 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 with the primary objective of assessing the safety profile of risdiplam in infants and determining 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 was 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). The study met its primary endpoint.
- 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. The study met its primary endpoint.
- 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. The study has completed recruitment (n=174).
- 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.