Data from Pivotal FIREFISH and SUNFISH Studies Demonstrate Clinical Benefit of Risdiplam in Type 1, 2, & 3 Spinal Muscular Atrophy Patients

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Babies with Type 1 SMA from Part 1 of FIREFISH continue to achieve motor milestones including standing
58% of patients experienced an improvement of at least 3 points on MFM32 scale vs. baseline after 12 months of treatment in Part 1 of SUNFISH
No drug related safety findings leading to withdrawal
NDA and MAA submissions planned for 2H2019

SOUTH PLAINFIELD, N.J., May 7, 2019 /PRNewswire/ -- PTC Therapeutics, Inc. (NASDAQ: PTCT) today announced clinical data from the studies of FIREFISH and SUNFISH demonstrating the benefit of risdiplam (RG7916) for the treatment of Type 1, 2 and 3 spinal muscular atrophy (SMA). Patients across all studies continue to achieve motor milestones relative to natural history. Risdiplam has been well tolerated at all doses across studies; there have been no drug related safety findings leading to withdrawal. Regulatory submissions based on Part 1 of FIREFISH and SUNFISH are planned in the second half of 2019. The data from these pivotal trials were presented at the 2019 American Academy of Neurology Annual Meeting in Philadelphia. The SMA program is a collaboration between PTC, the SMA Foundation, and Roche.

"The magnitude of the benefit observed in all SMA types in both trials is very compelling," said Stuart W. Peltz, Ph.D., Chief Executive Officer of PTC Therapeutics. "We believe the improvements seen in developmental milestones across patients with Type 1, 2 and 3 SMA, and the positive safety profile of risdiplam, an oral therapy, will support a compelling submission package for the FDA and the EMA."

In Part 1 of the FIREFISH study, at 12 months of treatment, among the infants who received the dose selected for the confirmatory Part 2 of the study, (n=17), 7 (41.2%) were able to sit without support for at least 5 seconds, assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development – Third Edition (BSID-III). In addition, 11 (64.7%) infants were able to sit (with or without support) while 9 (52.9%) achieved upright head control after 12 months of treatment as assessed by the Hammersmith Infant Neurological Examination Module 2 (HINE-2). Finally, 1 infant (5.9%) achieved the milestone of standing (supports weight) by this 12-month time point. These results demonstrate a clear divergence from natural history where babies with Type 1 SMA never achieve these milestones. No baby has required tracheostomy, reached permanent ventilation or lost the ability to swallow. At 12 months, 18/19 babies were able to feed orally (exclusively or in combination with a feeding tube). 85.7% of babies remain alive with three having discontinued due to the fatal progression of their disease.

Part 1 of SUNFISH includes a broad patient population aged 2-25 years with Type 2 or 3 SMA and with baseline functional status ranging from individuals unable to sit to those capable of walking. Scoliosis ranged from none to severe. An exploratory efficacy analysis of Part 1 of the SUNFISH study assessed motor function, using the Motor Function Measure-32 (MFM32) scale. The results demonstrate that among the patients for which the MFM32 test has been completed at all visits up to month 12 (n=43), 58% saw an improvement of at least 3 points on the scale from baseline, compared to 7.6% for a matched natural history cohort (n=39). The change from baseline in total MFM32 score is the primary efficacy endpoint in the ongoing Part 2 of the trial. In addition, a sustained median increase from baseline in SMN protein of greater than two-fold, as measured in blood, was seen after 12 months of treatment with risdiplam.

Risdiplam is an investigational small molecule SMN2 splicing modifier targeting the survival motor neuron 2 (SMN2) RNA, restoring a functional transcript. In preclinical studies, risdiplam given orally, crossed the blood brain barrier, and showed systemic distribution to all organs and tissues.

The table below depicts improvements across the FIREFISH and SUNFISH dose-finding studies after 12 months of treatment:

FIREFISH (	
Motor milestone achievement	• 9 infants (53%) were able to maintain an upright head position (HINE-2, n=17) • 10 infants (59%) demonstrated rolling (rolling to the side, prone to supine, or supine to prone) (HINE-2, n=17) • 7 infants (41%) were able to sit without support for at least 5 seconds (BSID-III, n=17) • 1 infant (6%) was able to stand (HINE-2, n=17)
Survival	• 85.7% (18/21) babies were event-free overall • Three infants experienced fatal complications of their disease after approximately 1, 8, and 13 months of treatment. None of these has been attributed by the investigator as related to risdiplam.
Pulmonary function and swallowing	• No baby has required tracheostomy, reached permanent ventilation or lost the ability to swallow
CHOP-INTEND	• 59% (11/17) achieved a score of 40 or above • Median change from baseline CHOP-INTEND score was 17.5

The most common adverse events included fever (pyrexia; 52.4%), upper respiratory tract infections (42.9%), diarrhea (28.6%), vomiting (23.8%), cough (23.8%) pneumonia (19.0%) and constipation (19.0%). No significant ophthalmological findings to date. Data cutoff 27 February 2019.

SUNFISH			
MFM32	Aged 2-11 (n=24)	Aged 12-25 (n=19)	Aged 2-25 (n=43)*
Total MFM change from baseline, **mean** (SD)	3.47 (3.77)	1.64 (3.43)	2.66 (3.70)
Total MFM change from baseline, **median** (range)	4.17 (-6.3, -9.4)	2.08 (-7.3, -6.3)	3.13 (-7.3, -9.4)
Proportion of patients who achieve improvement (i.e. a change from baseline in MFM score ≥3), % (n)	70.8 (17/24)	42.1 (8/19)	58.1 (25/43)

*Excludes 7 patients who performed the MFM20 assessment (only patients who performed the full MFM32 assessment are included in the analysis) and one patient who had dropped out of the study prior to the Month 12 visit.

The most common adverse events in Part 1 of the SUNFISH study were fever (pyrexia; 41%), cough (33%), vomiting (29%), upper respiratory tract infections (26%), persistent sore throat (oropharyngeal pain; 22%) and cold (nasopharyngitis; 20%). The most common serious adverse event that occurred in two of the 51 patients exposed to risdiplam was pneumonia. To date there have been no treatment-related safety findings leading to withdrawal from any study. No significant ophthalmological findings to date. Data cutoff 09 January 2019.

About Spinal Muscular Atrophy (SMA)
Spinal muscular atrophy (SMA) is a genetic neuromuscular disorder that is the leading genetic cause of mortality in infants and toddlers caused by deletion or mutation in the survival of motor neuron 1 (SMN1) gene, which results in reduced levels of SMN protein. The related SMN2 pre-mRNA is alternatively spliced producing only small amounts of functional SMN protein. Insufficient levels of SMN protein result in the progressive loss of motor neurons leading to muscle atrophy and death in its most severe form. It is estimated that 1 in every 11,000 newborn children will develop SMA.

About the SMA Clinical Trials
FIREFISH: An open-label, two-part clinical trial. Part 1 was a dose finding study in 21 infants and is now in the open label extension phase. 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 single-arm study using the dose selected in Part 1 in 41 infants with Type 1 SMA for 24 months, followed by an open label extension.

SUNFISH: A double-blind, two-part, placebo-controlled trial. Part 1 enrolled patients with Type 2 or 3 SMA to evaluate the safety, tolerability, and PK/PD of several risdiplam dose levels. The pivotal SUNFISH Part 2, in non-ambulant patients with Type 2 or 3 SMA, is evaluating safety and efficacy of the risdiplam dose level selected from Part 1 for 24 months, followed by an open label extension. This study has finished recruiting globally.

JEWELFISH: An ongoing, exploratory, open-label study to establish the safety and tolerability of risdiplam in people with SMA who have previously participated in a study with another therapy to treat SMA.

RAINBOWFISH: An open-label, single-arm, multicenter clinical study to investigate the efficacy, safety, pharmacokinetics, and pharmacodynamics of risdiplam in infants aged from birth to 6 weeks who have been genetically diagnosed with SMA but are not yet presenting with symptoms.

About the SMA collaboration
The SMA program was initiated by PTC Therapeutics in partnership with the SMA Foundation in 2006. In November 2011, Roche gained an exclusive worldwide license to the PTC/SMA Foundation SMN2 alternative splicing program. The development of risdiplam RG7916 is being executed globally by Roche, including in the US through Genentech, a member of the Roche group. The SMA program is overseen by a Joint Steering Committee with members from PTC, Roche, and the SMA Foundation.

About PTC Therapeutics, Inc.
PTC is a science-led, 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 pipeline of transformative medicines and our mission to provide access to best-in-class treatments for patients who have an unmet medical need.

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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: any advancement of the joint development program in SMA with PTC, Roche, and SMAF, in particular as related to the timing of enrollment, completion and evaluation of the Phase 2 clinical studies of risdiplam in SMA patients and the period during which the results of the studies will become available; the clinical utility and potential advantages of risdiplam, including its potential to impact every aspect of the disease; the timing and outcome of the regulatory strategy and process for risdiplam, including any potential regulatory submissions; PTC's strategy, future expectations, plans and prospects, future operations, future financial position, future revenues or projected costs; and the objectives of management. Other forward-looking statements may be identified by the words "potential," "will," "promise," "expect," "plan," "target," "anticipate," "believe," "estimate," "intend," "may," "project," "possible," "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 availability of data from either the SUNFISH or FIREFISH studies and the outcome of such studies; events during, or as a result of, these studies that could delay or prevent further development of risdiplam, including future actions or activities under the SMA joint development program; our expectations for regulatory approvals; PTC's scientific approach and general development progress; and the factors discussed in the "Risk Factors" sections 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, including with respect to PTC's joint development program in SMA with Roche and the SMAF. There are no guarantees that any product candidate under the joint development program will receive regulatory approval in any territory or prove to be commercially successful.

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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