Risdiplam Demonstrates Preliminary Evidence of Clinical Benefit in Type 1, 2, & 3 Spinal Muscular Atrophy Patients

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- Babies from FIREFISH Part 1 study showed increased survival & gains in developmental milestones -

- SUNFISH Part 1 study demonstrated a 3.1-point increase in motor function as measured by MFM32 -

- Pivotal portion of SUNFISH Part 2 study in Type 2 & 3 patients has completed enrollment -

SOUTH PLAINFIELD, N.J., Oct. 3, 2018 /PRNewswire/ -- PTC Therapeutics, Inc. (NASDAQ: PTCT) today announced interim clinical data from the Part 1, open-label studies of FIREFISH and SUNFISH demonstrating the benefit of risdiplam (RG7916) for the treatment of Type 1, 2 and 3 spinal muscular atrophy (SMA). The results showed that patients across all SMA types benefited from an oral systemic therapy indicated by increases in developmental motor milestones. Risdiplam was well tolerated at all doses across studies to date and no participants have withdrawn due to drug-related safety findings. The pivotal portions of both studies are ongoing. The data were presented at the 23rd International Annual Congress of the World Muscle Society in Argentina. The SMA program is a collaboration between PTC, the SMA Foundation, and Roche.

"The emerging results from FIREFISH and SUNFISH trials support the broad clinical benefit of a systemic oral treatment for SMA patients," said Stuart W. Peltz, Ph.D., Chief Executive Officer of PTC Therapeutics. "Patients with Type 2 and 3 SMA typically decline over the course of a year and the increase in motor function by over 3 points in SUNFISH when compared to natural history is exceptionally encouraging. We are excited by the gains in developmental motor milestones exhibited by Type 1 babies in FIREFISH. The observation of six babies sitting to date in a dose finding study is remarkable. SMA is a systemic disease, and risdiplam which is an oral treatment that reaches all affected organs has the potential to be a best-in-class therapy."

In Part 1 of the FIREFISH study, at Day 245 of treatment, 43% (6/14) of infants were able to sit (with or without support), including three who achieved unassisted sitting. Natural history indicates that Type 1 SMA babies never achieve this milestone. Ninety percent of babies remain alive with two having discontinued due to the fatal progression of their disease. In Part 1 of the SUNFISH study in Type 2 and 3 SMA patients, 63% (19/30) of patients treated with risdiplam for at least one year achieved a median increase in motor function (as measured by MFM32) of 3.13 points versus baseline. Typically patients with Type 2 or 3 SMA decline by 0.85 to 0.67 point per year[1]. In addition, median SMN protein level increases of greater than 2-fold were sustained over 12 months.

The pivotal portion of the SUNFISH clinical study has completed enrollment. Part 2 of SUNFISH is a randomized, double-blinded, multi-center, placebo-controlled study which enrolled 180 Type 2 and Type 3 SMA patients 2-25 years of age for 24 months, followed by an open-label extension. Patients enrolled in the SUNFISH trial have a broad age range (2-24 years; median age 8 years) and with broad functional characteristics. The primary endpoint is change from baseline in the total Motor Function Measure 32 (MFM-32) score at Month 12.

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, which was given orally, crossed the blood brain barrier, and showed systemic distribution to the organs that are affected by low levels of SMN protein.

The table below depicts improvements across the FIREFISH and SUNFISH dose-finding studies:

FIREFISH	
Outcome	Result
Sitting after 8 months of treatment (n=14)	• 6 infants (43%) sit with or without support including 3 infants (21%) who sit without assistance
Motor milestone achievement after 8 months of treatment (n=14)	• 10 infants (71%) achieved full or partial head control including 6 (43%) babies with upright head control • 7 infants (50%) kicking • 4 infants (29%) demonstrated rolling to the side
Survival	• 90% (19/21) babies were event-free vs. 50% of age-matched SMA Type 1 babies in natural history studies
Pulmonary function and swallowing	• No baby has required tracheostomy, reached permanent ventilation or lost the ability to swallow (Latest visit day - 546 days)
CHOP-INTEND	• Increases over time – from 5.5 points median at Day 56 (n=20) to 16 points median at Day 245 (n=14) • Increases in younger and older patients – 18.5 points median for babies 3-5 months old (n=4) and 14.5 points median for babies 5-7 months old (n=10) at Day 245 • 13 infants (93%) achieved ≥4-point increase (n=14) at Day 245

	• 8 infants (57%) achieved a score of 40 or above (n=14) at Day 245

The most common adverse events were fever (pyrexia: 52.4%,) diarrhea (26.8%), upper respiratory tract infections (19%), ear infections (14.3%), pneumonia (14.3%), constipation (14.3%), vomiting (14.3%), cough (14.3%) and upper respiratory inflammation (14.3%). Data cutoff: 7-Sept 2018.

SUNFISH			
Endpoint: (at 12 months of treatment)	>12 months Treatment		
MFM	All patients (n=30) *	Aged 2-11 (n=17)	Aged 12-24 (n=13)
Total MFM change from baseline, mean (SD)	2.47 (4.17)	3.31 (4.5)	1.36 (3.57)
Total MFM change from baseline, median (range)	3.13 (-7.3-11.5)	4.17 (-6.3-11.5)	2.08 (-7.3-5.2)
Proportion of patients who achieve improvement (i.e. a change from baseline in MFM score ≥3), % (n)	63.3 (19/30)	76.5 (13/17)	46.2 (6/13)

*Excludes 4 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. Serious adverse events that occurred in two or more of the 51 patients were nausea (4%), upper respiratory tract infection (4%), and vomiting (4%). Data cut-off 6th July 2018.

For more information on the Congress, visit http://www.wms2018.com/

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 a missing or defective survival of motor neuron 1 (SMN1) gene, which results in reduced levels of SMN protein. The homologous SMN2 pre-mRNA is predominantly spliced to a truncated mRNA, and only produces small amounts of functional SMN protein. Insufficient levels of SMN protein are responsible for the loss of motor neurons within the spinal cord leading to muscle atrophy and death in its most severe form. It is estimated that this devastating disease affects 1 in every 11,000 children born.

About the SMA Clinical Trials
FIREFISH: An open-label, two-part clinical trial. 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 single-arm study with the dose selected in Part 1 in approximately 40 infants with Type 1 SMA for 24 months, followed by an open-label extension. This study is recruiting globally.

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 targeting SMN2 splicing.

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. Founded 20 years ago, PTC Therapeutics has successfully launched two rare disorder products and has a global commercial footprint. This success 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:
All statements, other than those of historical fact, contained in this press release, 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 PTC's regulatory strategy and process; 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 initiation, 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.

[1] Vuillerot, C., et al. Responsiveness of the Motor Function Measure in Patients with Spinal Muscular Atrophy. Archives of Physical Medicine and Rehabilitation. 2013; 94: 1555-61.

View original content:http://www.prnewswire.com/news-releases/risdiplam-demonstrates-preliminary-evidence-of-clinical-benefit-in-type-1-2--3-spinal-muscular-atrophy-patients-300723444.html

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