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Orally delivered compounds, which selectively modify RNA splicing prevent deficits in mouse models of Spinal Muscular Atrophy

-Results published in Science show small molecule SMN2 splicing modifiers to be effective in SMA mouse models-

SOUTH PLAINFIELD, NJ - AUGUST 7, 2014 - Today the journal Science published results of a preclinical study demonstrating that treatment with orally available RNA splicing modifiers of the SMN2 gene starting early after birth is preventing deficits in mouse models of Spinal Muscular Atrophy (SMA). Scientists from Roche Pharma Research and Early Development (pRED), PTC Therapeutics, Inc., the SMA Foundation, the University of Southern California and Harvard University collaborated to demonstrate that continuous treatment of SMA mice with these compounds increased life span, normalized body weight and prevented both disease-related motor dysfunction and neuromuscular deficits in a mouse model of SMA. To view the animation related to the study, please visit: [SMA video](#)

"The investigational compounds used in this study represent the first orally available SMN2 splicing modifiers for SMA," commented Stuart W. Peltz, CEO of PTC Therapeutics, Inc. "Using the experience and expertise in RNA biology we have gained at PTC over the last 16 years, we used our alternative splicing technology to identify and subsequently optimize investigational compounds that target the SMN2 splicing to produce the SMN protein. Our unique partnership with Roche and the SMA Foundation has allowed this project to rapidly move into clinical development."

"Although still preclinical, these results demonstrate how SMN2 splicing modifiers could correct the molecular deficit that causes SMA," said Luca Santarelli, Head of Neuroscience, Ophthalmology and Rare Diseases at Roche. "This study represents an important step towards developing a potential therapeutic option for this devastating and currently untreatable condition. Early clinical trials are currently underway to determine the safety and tolerability of this approach."

The study used chemical screening and optimization to identify orally available small molecules that selectively alter the splicing of the SMN2 pre-mRNA to produce stable full-length SMN protein. The SMN2 splicing modifiers described in the Science article penetrated into all mouse tissues tested including brain, spinal cord and muscle, and thus improved SMN2 RNA splicing to increase SMN protein production in these disease-relevant tissues. As a result of the SMN protein increase, the compounds prevented the progression of SMA in a severe mouse model. These compounds also corrected SMN2 RNA splicing and increased SMN protein levels in cell cultures obtained from SMA patients, including stem cell-derived motor neurons. A Phase I clinical program to assess safety and tolerability with investigational compounds was initiated in early 2014.

"The findings of this preclinical study contribute significantly to our understanding of SMA and provide further evidence suggesting that our strategy to upregulate SMN with small molecules could be effective," said Loren Eng, President of the SMA Foundation. "We are proud to have seeded this important work – we believe it could have a meaningful impact on the lives of patients who suffer from SMA."

SMA is a genetic disease caused by mutation or deletion of the SMN1 (survival of motor neuron) gene. It affects one in approximately 10,000 live births and in the most severe forms is associated with a high rate of childhood mortality. SMA is characterized by progressive loss of motor neurons, muscle weakness and atrophy. The disease affects mainly proximal muscles including intercostal muscles (chest muscles), and patients often die due to respiratory complications.

About PTC Therapeutics

PTC is a biopharmaceutical company focused on the discovery and development of orally administered, proprietary small molecule drugs that target post-transcriptional control processes. Post-transcriptional control processes regulate the rate and timing of protein production and are essential to proper cellular function. PTC's internally discovered pipeline addresses multiple therapeutic areas, including rare disorders, oncology and infectious diseases. PTC has developed proprietary technologies that it applies in its drug discovery activities and in collaborations with leading biopharmaceutical companies. For more information on the company, please visit our website www.ptcbio.com.

About The SMA Foundation

Founded in 2003, the Spinal Muscular Atrophy Foundation is a nonprofit organization dedicated to accelerating progress towards a treatment for Spinal Muscular Atrophy through targeted funding of clinical research and novel drug development efforts. Since its inception, the Foundation has awarded over \$100 million for SMA research. The SMA Foundation serves as the hub and clearinghouse of information for the diverse universes involved in drug development, including pharmaceutical and

biotech companies, academia, non-profits, clinicians, patients, government/regulators, and the media. In addition, the Foundation is committed to raising awareness and generating support for increased research efforts in SMA among the leaders of industry and government. For more information, visit the SMA Foundation website at www.smafoundation.org.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. Twenty-four medicines developed by Roche are included in the World Health Organisation Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and chemotherapy. In 2013 the Roche Group employed over 85,000 people worldwide, invested 8.7 billion Swiss francs in R&D and posted sales of 46.8 billion Swiss francs. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority stakeholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

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PTC Therapeutics, Inc. Forward Looking Statements:

Any statements in this press release about future expectations, plans and prospects for PTC, the development of and potential market for PTC's product candidates, our clinical trials for lead compounds targeting SMA, our collaboration in SMA with Roche and the SMA Foundation, our current and planned regulatory submissions, our earlier stage programs, and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan" "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Forward-looking statements involve substantial risks and uncertainties that could cause our future results, performance or achievements to differ significantly from those expressed or implied by these forward-looking statements. Such risks and uncertainties include, among others, those related to the initiation and conduct of clinical trials, availability of data from clinical trials, expectations for regulatory approvals, our scientific approach and general development progress, the availability or commercial potential of our product candidates and other factors discussed in the "Risk Factors" in the most recent Quarterly Report, which is on file with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent PTC's views only as of the date of this press release. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing PTC's views as of any date subsequent to the date of this press release.