

**FOR IMMEDIATE RELEASE**

**Acetylon Pharmaceuticals Presents Preclinical Data for Selective HDAC1/2 Inhibitors for the Treatment of Sickle Cell Disease and  $\beta$ -Thalassemia at the American Society of Hematology Annual Meeting**

**Boston – December 9, 2013** – [Acetylon Pharmaceuticals](#), Inc., the leader in the development of selective histone deacetylase (HDAC) inhibitors for enhanced therapeutic outcomes, announced that positive preclinical data for its selective HDAC1/2 inhibitors for the treatment of sickle cell disease (SCD) and  $\beta$ -thalassemia (bT) were presented at the 55<sup>th</sup> Annual Meeting of the American Society of Hematology (ASH) in New Orleans, LA. An oral presentation given today and a poster presentation on December 8 describe the mechanism of action of selective HDAC1/2 inhibition in the induction of fetal hemoglobin (HbF) and report that Acetylon's selective HDAC1/2 inhibitor compounds may provide a novel treatment option for SCD/bT.

"Inhibition of Class I HDACs is known to induce HbF, however, significant toxicity, potentially through the inhibition of HDAC3, has limited the development of non-selective HDAC inhibitors for the treatment of SCD/bT," said Matthew Jarpe, Ph.D., Senior Director of Biology at Acetylon. "In the data presented at ASH, Acetylon's selective HDAC1/2 inhibitors induced HbF through the downregulation of known repressors of fetal globin synthesis and the upregulation of proposed activators of fetal globin synthesis with minimal effect on cell viability. Together, the data suggest that HDAC1/2 inhibition may provide a novel, targeted treatment option for patients with SCD and bT."

**Highlights of the Presentations at ASH**

*Pharmacological Inhibition of Histone Deacetylase (HDAC) 1, 2 or 3 Have Distinct Effects on Cellular Viability, Erythroid Differentiation, and Fetal Globin (HbG) Induction (oral presentation, [Abstract # 564](#))*

- Selective HDAC1/2 inhibition resulted in a 3-fold increase in HbG
- Inhibition of HDAC 1, 2 and 3 resulted in a 20-fold decrease in cell viability, whereas selective inhibition of HDAC 1 and 2 resulted in a minimum reduction of cell viability (1.2-fold)

*Mechanistic Insights into Fetal Hemoglobin (HbF) Induction through Chemical Inhibition of Histone Deacetylase 1 and 2 (HDAC1/2) (poster presentation, [Abstract # 2253](#))*

- Selective HDAC1/2 inhibition resulted in the downregulation of genes known to repress fetal globin synthesis (Bcl11A and Sox6) and upregulation of genes proposed to activate fetal globin synthesis (Klf2 and Gata2)

**About HDAC1/2 Inhibition**

The induction of fetal hemoglobin (HbF) is an established therapeutic strategy for sickle cell disease that also holds potential for the treatment of beta-thalassemia. HDAC inhibition has been shown to induce HbF, however, clinical development of non-selective HDAC inhibitors has been limited due to off-target



side effects. Selective HDAC1/2 inhibition represents a novel treatment approach that could potentially represent a better tolerated treatment option for patients with SCD and bT.

### **About Acetylon**

Acetylon Pharmaceuticals, Inc., based in Boston, Massachusetts, is a leader in the development of novel small molecule drugs targeting epigenetic mechanisms for the enhancement of therapeutic outcomes in cancer and other critical human diseases. The Company's epigenetic drug discovery platform has yielded a proprietary portfolio of optimized, orally-administered Class I and Class II histone deacetylase (HDAC) selective compounds. Alteration of HDAC regulation through selective HDAC inhibition is thought to be applicable to a broad range of diseases including cancer, sickle cell disease and beta-thalassemia, and autoimmune and neurodegenerative diseases. Acetylon's lead drug candidate, ricolinostat (ACY-1215), is a selective HDAC6 inhibitor currently in Phase 1b clinical development for the treatment of multiple myeloma. The Company recently announced a strategic collaboration agreement with Celgene Corporation, which includes an exclusive option for the future acquisition of Acetylon by Celgene. Acetylon's scientific founders are affiliated with the Harvard University, the Dana-Farber Cancer Institute, the Massachusetts General Hospital, and Harvard Medical School. [www.acetylon.com](http://www.acetylon.com)

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