Acetylon Presents Preclinical Data Demonstrating the Utility of Selective HDAC1,2 Inhibition by ACY-957 to Induce Gamma Globin (HBG) Protein Expression for the Treatment of Sickle Cell Disease and Beta-Thalassemia

-- Results will be presented in an oral presentation at the 58th Annual Meeting of the American Society of Hematology (ASH) --

BOSTON – December 4, 2016 – Acetylon Pharmaceuticals, Inc., the leader in the development of selective histone deacetylase (HDAC) inhibitors for enhanced therapeutic outcomes, today announced that it will present preclinical data comparing the effects of alternative dosing schedules for the selective HDAC1,2 inhibitor, ACY-957, on gamma globin (HBG) protein expression. In an oral presentation at the American Society of Hematology Annual Meeting (ASH) in San Diego, California, Jeffrey R. Shearstone, Ph.D., Associate Director of Biology at Acetylon, will present data demonstrating that treatment with ACY-957 was well tolerated in a 3-week dosing regime and led to greater than 50-fold increases of HBG mRNA and protein in non-anemic primates.

Acetylon is developing selective HDAC1,2 inhibitors for the treatment of sickle cell disease and beta-thalassemia, two blood disorders with the highest prevalence worldwide of any human genetic disease. When paired with alpha globin, gamma globin (HBG) protein forms fetal hemoglobin (HBF), which can substitute for defective adult hemoglobin found in sickle cell and β-thalassemia patients to ameliorate disease symptoms. Acetylon has previously shown that ACY-957 induces HBG mRNA and HBF protein *in vitro* and that 5 sequential days of oral dosing with ACY-957 is sufficient to induce potentially therapeutic levels of HBG mRNA in the blood of non-anemic primates – the first such demonstration.

The preclinical study being presented at ASH investigated the effects of ACY-957 over an extended dosing period and with alternative dosing schedules. Results from the study demonstrate that treatment with ACY-957 in non-anemic primates was well tolerated in a 3-week dosing regimen and that pharmacologic inhibition of HDAC1,2 by ACY-957 led to a substantial increase in HBG mRNA and protein. Furthermore, dosing for 3 days followed by a 4-day break (3-on-4-off dosing) yielded a pharmacodynamic (PD) and HBG induction response that was comparable to 5-on-2-off dosing with a minor impact on body weight and reduced impact on hematopoiesis. These data suggest that dose level and schedule may be further refined in human clinical trials to optimize the therapeutic window of selective HDAC1,2 inhibitors while accomplishing substantial induction of fetal hemoglobin to treat hemoglobinopathies.

“These *in vivo* data validate HDAC1,2 inhibition as a therapeutic target,” said Dr. Shearstone. “With greater insight into the pharmacodynamic response of a 3-on-4-off dosing schedule, we plan to develop potential clinical candidates in the coming year and to further refine the dose and schedule to increase the therapeutic window. While others have shown that HBG and HBF can be induced *in vitro* by non-selective histone deacetylase (HDAC1,2,3) inhibitors, such approaches would likely be clinically associated with significant toxicity and adverse events, and we anticipate that selective HDAC1,2 inhibition will provide a superior treatment option that minimizes potential side effects.”

Details of the presentation are as follows:

Title: The Histone Deacetylase 1 and 2 (HDAC1/2) Inhibitor ACY-957: Impact of Dosing Schedule on Pharmacokinetics (PK), Pharmacodynamics (PD), Hematopoietic Toxicity, and Gamma Globin (HBG, ɣ) Expression in Monkey

Date: Sunday, December 4, 2016

Time: 10:30 AM

Location: Room 7AB (San Diego Convention Center)

Session: 112. Thalassemia and Globin Gene Regulation: Fetal Hemoglobin Regulation

Abstract Number: 323

About Acetylon

Acetylon Pharmaceuticals, Inc., based in Boston, Massachusetts, is the leader in the development of novel, selective 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 Class I and Class II histone deacetylase (HDAC) selective compounds for oral administration. Alteration of HDAC regulation through selective HDAC inhibition is thought to be applicable to a broad range of diseases including cancer, autoimmune and neurodegenerative diseases, neuropathy, and hemoglobinopathies including sickle cell disease and beta-thalassemia. www.acetylon.com

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