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Acetylon Pharmaceuticals Highlights Positive Interim Phase 1b Clinical Data of Ricolinostat (ACY-1215) in Multiple Myeloma at the American Society of Hematology Annual Meeting

--Additional Preclinical Data Presented on Ricolinostat in Potential New Drug Combinations and HDAC6 Biomarkers in Multiple Myeloma--

Boston – December 9, 2013 – Acetylon Pharmaceuticals, Inc., the leader in the development of selective histone deacetylase (HDAC) inhibitors for enhanced therapeutic outcomes, today announced that positive interim clinical data from the two proof-of-concept clinical trials with selective HDAC6 inhibitor, ricolinostat (ACY-1215), were presented at the 55th Annual Meeting of the American Society of Hematology (ASH) in New Orleans, LA. The two trials are the Phase 1b dose escalation portion of a Phase 1/2 study of ricolinostat in combination with bortezomib (Velcade®) and dexamethasone and a Phase 1b dose escalation study of ricolinostat in combination with lenalidomide (Revlimid®) and dexamethasone, both for the treatment of patients with relapsed or refractory multiple myeloma (MM).

Data from the combination study including ricolinostat and lenalidomide was presented in a poster session on Sunday, December 8 and appeared particularly promising with no dose-limiting toxicities to date. All 16 (100%) of the evaluable patients experienced clinical benefit (disease stabilization or better) and 11 patients (69%) responded to therapy (partial response or better). The most common treatment emergent adverse events (AEs) were fatigue, upper respiratory infection, neutropenia, headache, diarrhea, and muscle spasms, all of which were mild or moderate in severity and without relationship to the dose of ricolinostat, and most were not considered related to ricolinostat.

Combination therapy including ricolinostat and bortezomib was also well tolerated, with primarily low grade and unrelated AEs of hematology changes, creatinine elevation, fatigue, decreased appetite, diarrhea and changes in laboratory investigations, with 12 out of 20 evaluable patients experiencing clinical benefit (60%) and 5 patients (25%) responding to treatment with a trend towards enhanced response at the highest dose. Data from this Phase 1/2 study were presented in an oral presentation on Monday, December 9. Clinical benefit has been durable in both studies, with patients remaining on treatment for up to 16 cycles of treatment (1 year) to date.

“Ricolinostat thus far has demonstrated an excellent safety profile, allowing physicians to keep patients on therapy for much longer than the traditional pan-HDAC inhibitors and explore the full potential that selective inhibition of HDAC6 can provide for patients with MM,” said Noopur Raje, MD, Associate Professor, Department of Medicine, Harvard Medical School, Director, Multiple Myeloma Program, Medical Oncology, Massachusetts General School, and investigator in both clinical studies of ricolinostat. “I am highly encouraged by the initial clinical response signals that we are seeing, both with lenalidomide and bortezomib, and believe that ricolinostat has the potential to become an important addition to combination regimens for the treatment of MM.”

Five additional poster presentations at ASH included data from preclinical studies with ricolinostat demonstrating highly synergistic activity in combination with three additional agents in models of MM: immunomodulatory drug (IMiD), pomalidomide (Pomalyst®), and proteasome inhibitors, carfilzomib (Kyprolis®) and ixazomib. Acetylon also presented data on the discovery of HDAC6 biomarkers, which could serve to guide further clinical development of ricolinostat.

"Ricolinostat's great synergy with IMiDs and proteasome inhibitors is exemplified by the early signs of clinical activity in our current clinical studies with lenalidomide and bortezomib, and we believe this profile is enhanced by these preclinical studies with the next-generation compounds, pomalidomide, carfilzomib and ixazomib," commented Catherine A. Wheeler, MD, Vice President, Clinical Development of Acetylon. "These data underscore our strategy to expand the clinical exploration of ricolinostat's potential in additional combinations and indications with the support of our collaboration with Celgene. We look forward to an exciting year in 2014, with the initiation of two additional clinical trials of ricolinostat in MM, and the completion of our current studies."

Highlights of the Presentations at ASH

ACY-1215, a Selective Histone Deacetylase (HDAC) 6 Inhibitor, in Combination with Lenalidomide and Dexamethasone (dex), is Well Tolerated without Dose Limiting Toxicity (DLT) in Patients (Pts) with Multiple Myeloma (MM) at Doses Demonstrating Biologic Activity: Interim Results of a Phase 1b Trial (poster presentation, Abstract # 3190)

- Ricolinostat has been studied in 22 patients in combination with lenalidomide (Revlimid®) and dexamethasone and has been shown to be well-tolerated, with no maximum tolerated dose (MTD) identified to date
- Of 16 patients evaluable for response, all 16 (100%) of the evaluable patients experienced clinical benefit (disease stabilization or better) and 11 patients (69%) responded to therapy (partial response or better). 1 CR (complete response), 3 VGPRs (very good partial response), 7 PRs (partial response) and 2 MRs (minimal response) were seen and 3 patients achieved SD (stable disease) as their best response
- The most common treatment emergent AEs, including fatigue (50% of patients), upper respiratory infection (39%), neutropenia (27.8%), headache, diarrhea, and muscle spasms (22.2% each) were mild or moderate in severity and there was no relationship to the dose of ricolinostat. Severe events were primarily hematologic, as well as fatigue and asymptomatic laboratory investigations; most were unrelated to ricolinostat

ACY-1215, a Selective Histone Deacetylase (HDAC) 6 Inhibitor: Interim Results of Combination Therapy with Bortezomib in Patients with Multiple Myeloma (MM) (oral presentation, Abstract # 759)

- Ricolinostat has been studied in 37 patients in a Phase 1 trial and has shown to be safe and well-tolerated, with no MTD yet identified

- Of 20 patients treated in Phase 1b with the combination of ricolinostat, bortezomib (Velcade®) and dexamethasone who are evaluable for response, 2 VGPRs, 3 PRs and 2 MRs were seen and 5 patients achieved SD as their best response
- Most adverse events were low grade, and included hematologic changes, elevation of creatinine, fatigue, loss of appetite, diarrhea, and changes in laboratory investigations; these were not increased at higher doses of ricolinostat and most were considered not related to ricolinostat

Preclinical Combination of the Oral Investigational Agents ACY-1215, a Selective HDAC6 Inhibitor, and Ixazomib, a Proteasome Inhibitor, Demonstrates Combination Benefit in Multiple Myeloma Cell Lines and Xenograft Models (poster presentation, Abstract # 4437)

- Ricolinostat in combination with oral proteasome inhibitor, ixazomib, demonstrated increased efficacy similar to combination with bortezomib both *in vitro* and *in vivo*
- *In vivo*, the combination of ricolinostat and ixazomib has striking antitumor activity, with regression of the xenograft tumors below starting volumes, a level maintained throughout the 17-day dosing period

Inhibition of Autophagy by ACY-1215, a Selective HDAC6 Inhibitor Accelerates Carfilzomib-Induced Cell Death in Multiple Myeloma (poster presentation, Abstract # 4431)

- Proteasome inhibition can trigger autophagy, thought to be one of the key mechanisms of cell survival and lead to resistance as is frequently seen with bortezomib
- Combination treatment of ricolinostat and carfilzomib (Kyprolis®) resulted in significant synergistic cytotoxic effects against several MM cell lines through ricolinostat's ability to potently regulate autophagy through HDAC6 inhibition. This may overcome proteasome inhibitor resistance in the clinic

ACY-1215, a First-In-Class Selective Inhibitor of HDAC6, Demonstrates Significant Synergy with Immunomodulatory Drugs (IMiDs) in Preclinical Models of Multiple Myeloma (MM) (poster presentation, Abstract # 1952)

- Combining ricolinostat with either lenalidomide (Revlimid®) or pomalidomide (Pomalyst®) leads to synergistic decreases in the viability of MM cells *in vitro* and decreased expression of critical cancer targets Myc and IRF4
- The combination of ricolinostat and either lenalidomide or pomalidomide was well tolerated *in vivo*

Tubulin Hyper-Acetylation in Blood Lymphocytes: Pharmacodynamic (PD) Biomarker for the Selective Histone Deacetylase (HDAC) 6 Inhibitor ACY-1215 in Multiple Myeloma (MM) Patients (poster presentation, Abstract # 3219)

- Acetylated α-tubulin as a clinical PD biomarker suggests (along with pharmacokinetic data) that ricolinostat reached a pharmacologically relevant level of HDAC6 inhibition at clinical doses ≥80 mg
- These results will aid in the determination of the recommended Phase 2 dose of ricolinostat in combination with proteasome inhibitors and IMiDs

Discovery Histone Deacetylase (HDAC)6 Specific Proteomic Biomarkers in Multiple Myeloma (MM) Using Stable Isotope Labeling by Amino Acids in Cell Culture (SILAC) (poster presentation, Abstract # 1909)

- With administration of ricolinostat, AcK peptides identified in MM cells by the SILAC approach confirmed the critical function of HDAC6 in protein folding, ubiquitination, degradation, cytoskeleton structure and apoptosis, and also suggested other new functional targets for HDAC6 inhibition
- AcK peptide biomarkers could expand knowledge of the role of HDAC6 inhibition, particularly in combination with other MM therapeutic agents and assist in the development of biomarkers of ricolinostat activity in patients with MM

About Ricolinostat

Blood cancers such as multiple myeloma and lymphoma are characterized by successive genetic mutations resulting in uncontrolled cell proliferation and dysfunctional production of intracellular proteins. Ricolinostat (ACY-1215) selectively inhibits the intracellular enzyme HDAC6, which leads to an accumulation of excess protein and in addition may disrupt critical proliferative signals in malignant cells. Disruption of these molecular processes in cancer cells triggers programmed cell death, called "apoptosis," with little or no effect on normal cells. Currently available HDAC drugs affect the expression of numerous genes in normal cells as well as cancer cells, which can result in side effects such as gastrointestinal dysfunction, lowered blood platelet levels and risk of hemorrhage and profound fatigue as well as potential for significant cardiac toxicity. Selective inhibition of HDAC6 is expected to reduce or eliminate these often-severe side effects associated with non-selective HDAC inhibition and may enable the development of optimized treatment regimens, including maximally effective combination drug therapies.

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

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