Regenacy Pharmaceuticals HDAC1,2 Inhibitors Demonstrate Single-agent and Synergistic Activity with Azacitidine (Vidaza®) in Preclinical Models of Acute Myeloid Leukemia

-- Results from studies in multiple in vitro, ex vivo and in vivo preclinical models of AML published online in PLOS ONE –

-- Regenacy to present at the Biotech Showcase-

BOSTON – January 11, 2017 – Regenacy Pharmaceuticals, LLC, a clinical-stage biopharmaceutical company regenerating biological function by protein acetylation, today announced the publication of results from preclinical studies that demonstrate potent anti-leukemic activities of HDAC1,2-selective inhibitors both as single agents and in combination with azacitidine (Vidaza®) in multiple models of acute myeloid leukemia (AML). The manuscript titled, "Selective inhibitors of histone deacetylases 1 and 2 synergize with azacitidine in acute myeloid leukemia," was published today in the online peer-reviewed journal *PLOS ONE* by researchers from the former Acetylon Pharmaceuticals. Regenacy was spun out from Acetylon in December 2016 prior to the acquisition of Acetylon by Celgene Corporation. Regenacy owns Acetylon's former portfolio of preclinical selective HDAC1,2 inhibitor candidates and patent families for development in all human disease indications including hematologic cancers. Simon S. Jones, Ph.D., Senior Vice President, Preclinical Development and Chief Operating Officer of Regenacy will present a corporate overview at 3:00 PM Pacific Time today, January 11, 2017, at the 9th annual Biotech Showcase being held at the Hilton San Francisco Union Square.

Abnormal epigenetic regulation is implicated as one of the underlying causes of AML, the most prevalent form of leukemia in adults. Inhibitors of two epigenetic enzymes, DNA methyltransferase and histone deacetylase (HDAC), have exhibited activity in preclinical AML models. Due to the heterogeneous nature of AML, it is believed that combination regimens will be necessary to achieve the desired clinical efficacy, however the toxicity profiles of non-selective HDAC inhibitors in the combination setting limit their clinical utility.

In this work, the authors describe the preclinical development of a series of selective inhibitors of HDAC1 and HDAC2, namely ACY-957 and ACY-1035, which are hypothesized to have improved safety profiles, for combination therapy in the treatment of AML. Selective inhibition of HDAC1 and HDAC2 was shown sufficient to achieve efficacy both as a single agent and in combination with the DNA methyltransferase inhibitor, azacitidine, in preclinical models of AML, including established AML cell lines, primary leukemia cells from AML patient bone marrow samples and *in vivo* xenograft models of human AML. The authors also conducted gene expression profiling of AML cells treated with either an HDAC1,2 inhibitor, azacitidine, or the combination of both. They successfully identified a list of genes involved in transcription and cell cycle regulation as potential mediators of the combinatorial effects of HDAC1,2 inhibition with azacitidine.

"Together, our findings demonstrate that selective HDAC1,2 inhibitors are efficacious both as single agents and in combination with azacitidine in inhibiting proliferation of AML cell lines and primary AML blasts from patient bone marrow samples," said Dr. Jones. "Importantly, these findings have laid a foundation for further investigations to characterize the pharmacology and therapeutic index of this combination in efficacy and toxicology studies, potentially supporting the initiation of human clinical trials. Furthermore, additional studies are warranted to explore the combination of selective HDAC1,2 inhibitors with a broadened range of existing and emerging therapies for AML as well as biologically related myelodysplastic syndromes (MDS)."

About Acute Myeloid Leukemia

Acute myeloid leukemia (AML) is a diverse group of cancerous disorders that affect the bone marrow and hematopoietic stem cells (the cells that differentiate to form blood cells) and is the most prevalent acute leukemia in adults. These disorders are characterized by defects in myeloid differentiation and increased proliferation of neoplastic hematopoietic precursor cells which block the production of normal blood cells. As a result, the number of healthy blood cells (red cells, white cells and platelets) is usually lower than normal, leading to a number of life-threatening conditions, including anemia (low red blood cell counts result in low blood oxygen levels), neutropenia (low white cell counts result in an ineffective immune system), and thrombocytopenia (low platelet counts can cause bleeding and easy bruising). Outcomes for patients with AML remain poor, highlighting the need for novel treatment options.

About Regenacy

Regenacy Pharmaceuticals, LLC is a clinical-stage biopharmaceutical company regenerating biological function by protein acetylation for the treatment peripheral neuropathies, cognitive disorders, hemoglobinopathies and oncology indications. The company's selective inhibition technology provides superior safety profiles and potential enhanced efficacy compared to non-selective HDAC inhibitors. Regenacy's programs selectively inhibit histone deacetylase 6 (HDAC6) to restore normal protein and organelle intracellular transport in diabetic and other peripheral neuropathies and ciliopathic/polycystic diseases, and selectively inhibit HDACs 1 and 2 to restore oxygen transport in orphan blood disorders such as sickle cell disease and beta-thalassemia, regenerate normal cognitive function in patients with psychiatric disorders, and restore normal bone marrow function through differentiation of acute myeloid leukemia (AML) cells. www.regenacy.com

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