Regenacy Pharmaceuticals

CORPORATE OVERVIEW

Winter 2017

Regenerating Normal Protein Function via Next-Generation Selective HDAC Inhibition

Regenacy Pharmaceuticals, LLC is a clinical-stage biopharmaceutical company developing treatments for peripheral neuropathies and hemoglobinopathies based on regeneration of normal protein function with oral, isoform selective histone deacetylase enzyme ("HDAC") inhibitors. Regenacy's selective inhibition technology provides superior safety profiles and potential enhanced efficacy compared to non-selective HDAC inhibitors.

Regenacy was recently spun-out from Acetylon Pharmaceuticals following the acquisition by Celgene of Acetylon and its oral HDAC6 selective inhibitor, citarinostat (ACY-241), for pivotal clinical trials in multiple myeloma. Regenacy received exclusive rights to Acetylon's orally bioavailable, HDAC6 selective inhibitor, ricolinostat (ACY-1215), for a range of non-cancer disease indications outside of Celgene's strategic areas of focus.

Ricolinostat is currently positioned to enter Phase 2 clinical trials in peripheral neuropathy based on compelling proof-of-concept preclinical studies, with first-in-class potential for regenerative disease modification. In addition, there are near term opportunities for ricolinostat in ciliopathic diseases including polycystic kidney disease and cholangiocarcinoma, based on promising preclinical proof-of-concept studies.

Ricolinostat has completed Phase 2 clinical trials in multiple myeloma and has been studied in a range of Phase 1 trials, comprising experience in more than 200 patients and including use both as a single agent and in combination with various anticancer agents. **Ricolinostat has demonstrated an excellent safety and tolerability profile in clinical trials, particularly when contrasted with the high toxicity of currently marketed pan-HDAC inhibitors (e.g. vorinostat, panobinostat).**

- **Phase 2-ready lead program (ricolinostat) in peripheral neuropathy**
- **Potential breakthrough treatments with ricolinosat in other diseases of high unmet need**
- **Validated preclinical HDAC1/2 inhibitor program in sickle cell disease and β-thalassemia**
- **Additional opportunities for HDAC1/2 inhibitors in oncology and cognitive dysfunction**

Ricolinostat is protected by issued US and foreign composition of matter patents through 2034, with additional method-of-use patents positioned to issue for diabetic, chemotherapeutic and inherited neuropathies, as well as for polycystic kidney disease.

Regenacy also received Acetylon's extensive, unparalleled portfolio of isoform-selective HDAC1/2 inhibitors, which have demonstrated preclinical proof-of-concept for the induction of fetal hemoglobin in primates and are targeted for clinical development in sickle cell disease and β-thalassemia in 2018. The HDAC1/2 program has further potential for treating cognitive dysfunction as well as in oncology. **Regenacy's isoform selective HDAC1/2 inhibitors are differentiated from pan-Class I (i.e. HDAC1/2/3) inhibitors by superior preclinical safety and tolerability profiles, and they include both blood-brain barrier penetrant and non-penetrant preclinical candidates formulated for oral administration as tablets, with excellent pharmacokinetic properties.**

Lead Programs Target both Major and Rare Diseases Having Critical Unmet Needs

Diabetic peripheral neuropathy (DPN) is one of the most common complications of diabetes. DPN causes burning pain, numbness, and tingling in the hands and feet. Current treatments address only the pain and are minimally effective, addictive, and/or poorly tolerated. There were an estimated 4.5 million cases of diabetic peripheral neuropathy in 2015 in the US and EU5. The drug-treated prevalence of DPN is expected to increase as diabetes affects a larger proportion of the population. Total current market size is estimated to be ~$12B for drugs that offer symptomatic relief of pain only, and has even greater potential for a disease modifying therapy. A further estimated 500,000 patients suffer from chemotherapy induced peripheral neuropathy (CIPN) and approximately 100,000 from Charcot-Marie-Tooth (CMT) disease and related inherited neuropathies.

Hemoglobinopathies, including sickle cell disease (SCD) and beta thalassemia (bT), make up the largest group of severe genetic diseases worldwide, together afflicting an estimated 150,000 SCD patients US/EU and 15,000 bT patients US/EU with a worldwide estimated incidence of 300,000 SCD/bT. There are few therapeutic options for these patients, and many are at risk for painful and life-threatening vaso-occlusive crises (SCD), and iron overload and other adverse consequences of repeated blood transfusion (bT), resulting in repeated hospitalization, organ failure and shortened life expectancy.

Cognitive dysfunction is a significant consequence of both neurodegenerative diseases, including Alzheimer's disease, and psychological disorders including schizophrenia and major depressive disorder. Improvements in cognition in both neurodegenerative diseases and psychological disorders are critical for patients to achieve improved function and quality of life, while reducing the financial burden of extended care. Acute myelogenous leukemia affects approximately 42,000 patients in the US and EU, with an additional 68,000 suffering from related myelodysplastic syndrome.

Broad, Maturing Portfolio of Selective HDAC Inhibitors

PRODUCT CANDIDATE	LEAD OPTIMIZATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3
HDAC6 Inhibitors					
Ricolinostat	Peripheral Neuropathies				Phase 2 POC Q2 2017
Ricolinostat	Polycystic Kidney Disease				Phase 2 POC Q4 2017
Ricolinostat	Cholangiocarcinoma				
HDAC1/2 Inhibitors					
Lead RCY-1497	Sickle Cell / β-Thalassemia				
Lead RCY-2014	Neurodegeneration / Psychiatric / Other				
Discovery Program	AML/MDS				

Robust Preclinical Proof-of Concept with Selective HDAC Inhibitors

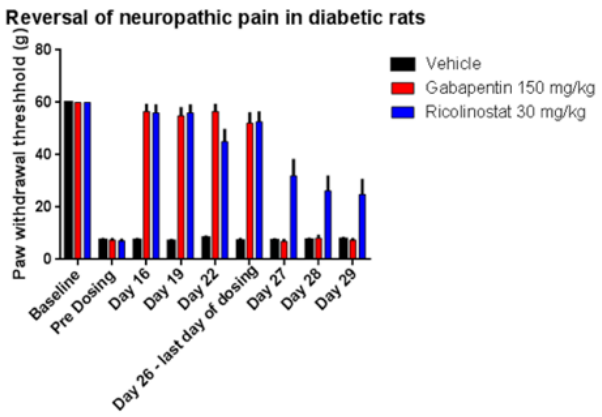
Ricolinostat reverses established diabetic neuropathic pain within hours of dosing (panel). The effect is similar to approved neuropathic pain treatments, gabapentin and pregabalin. However the effect persists for days after the drug is cleared, unlike standard analgesics. In addition ricolinostat reverses chemotherapy (e.g. taxane and cisplatin) induced neuropathy, and it restores motor function and nerve conductance velocity in a mouse model of Type II Charcot-Marie-Tooth disease.

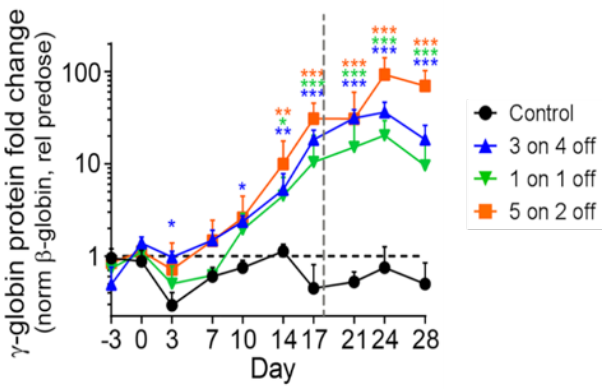
Ricolinostat has potential to treat not only peripheral neuropathic pain but also other symptoms of neuropathy, including numbness / loss of sensation and tingling – and the effect may be disease modifying, as evidenced in preclinical disease models

A favorable pre-IND meeting with FDA's Analgesia, Anesthesia and Addiction Products Division was held in September, 2016. Accordingly, an IND application has been prepared and is ready for submission and initiation of a proof-of-concept randomized controlled Phase 2 trial of ricolinostat in diabetic peripheral neuropathy during H2 2017.

Selective HDAC1/2 inhibition induces, in a non-anemic primate model of human globin induction, a robust increase of γ-globin mRNA and subsequent 40-100 fold increase in γ-globin mRNA (panel) with the proof-of-concept compound ACY-957, under a variety of dosing condtions. Notably γ-globin protein levels remained elevated after cessation of dosing (panel, day 17 dashed line). Also γ-globin mRNA and fetal hemoglobin is induced in red blood cell progenitors from SCD and bT patients by HDAC1/2 inhibition. **This work was presented orally at the 2016 American Society of Hematology Annual Conference and also published in PLOS ONE 2016.**

Several lead drug candidates have been identified (**ACY-1497** and others) for additional preclinical validation and planned entry into IND enabling studies during 2017, and for planned initiation of human clinical trials in early 2018.





Leadership Team With Extensive Neurology, Hematology & Small Molecule Expertise

MANAGEMENT TEAM

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SCIENTIFIC ADVISORS

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