Nimbus Therapeutics Announces Initiation of Clinical Studies For ACC Inhibitor

Upcoming AACR and EASL poster presentations support Nimbus' novel, liver-directed approach to allosteric ACC inhibition across liver disease spectrum, including NASH and HCC

Cambridge, Mass., April 21, 2015—Nimbus Therapeutics announced today that it has initiated a Phase I clinical program for NDI-010976, an allosteric Acetyl CoA Carboxylase (ACC) inhibitor, for the treatment of non-alcoholic steatohepatitis (NASH) and related fatty liver disease-spectrum disorders. The single site, open-label Phase I study is being conducted in healthy human volunteers to assess the safety, pharmacokinetic (PK) behavior and maximum tolerated dose of NDI-010976. A subsequent Phase Ib study will enroll obese patients with metabolic syndrome in order to measure key pharmacodynamic (PD) markers that are relevant to the NASH patient population. Nimbus expects all Phase I studies will be completed this year and Phase II studies will begin early next year.

"We believe that ACC inhibition offers a potentially novel and important approach to the treatment of NASH and related disorders since it precisely targets a key enzyme which is required for the formation of lipids that accumulate in the liver during NASH that drive pathogenesis of the disease," said Don Nicholson, Ph.D., Chief Executive Officer at Nimbus. "Furthermore, our preclinical data demonstrate that the effects of ACC inhibition extend to reducing inflammation and limiting fibrosis, which are hallmarks of NASH progression. We look forward to sharing these data with the scientific and medical community as we progress NDI-010976 through clinical development."

NDI-010976 represents the first liver-targeted allosteric inhibitor of ACC intended for the treatment of NASH, an increasingly common, serious liver disease which is estimated to affect 16 million Americans.[1] NASH can lead to liver cirrhosis, often resulting in the need for a liver transplant, as well as other complications including hepatocellular carcinoma (HCC), a liver cancer with high mortality rates. Currently there are no therapies specifically approved to treat NASH, and limited options for patients with advanced HCC, and there are no other ACC inhibitors publicly disclosed to be in development for these diseases. In addition to NDI-010976, Nimbus is continuing to advance a pipeline of novel small molecules, including those for IRAK4, Tyk2, KRas and other medically important targets.

[1]Frontline Gastroenterol. 2014 Jul; 5(3): 211-218; Aliment Pharmacol Ther. 2011 Aug; 34(3): 274-85; World J Transplant. 2014 Jun 24; 4(2): 81-92; Hematology. 2014 Dec 29

Upcoming Poster Presentations

American Association of Cancer Research (AACR) Annual Meeting
April 18 – 22, 2015; Philadelphia, Penn.
Poster Title: Liver selective acetyl-CoA carboxylase inhibition by ND-654 improves survival in cirrhotic rats with hepatocellular carcinoma
Presentation Date and Time: Tuesday, April 21, 2015; 1:00 – 5:00 p.m. ET
Abstract #4452, Section 30, Poster Board #9

Nimbus, in collaboration with researchers from Massachusetts General Hospital, previously presented data (PDF File) demonstrating that daily oral administration of its ACC inhibitor ND-654 reduced tumor incidence by 55 percent in an animal model of cirrhosis and HCC. At today's poster session, the researchers will present data showing that ND-654 significantly improved median survival time in this model, decreased tumor cell proliferation, induced tumor necrosis and decreased fibrosis.

European Association for the Study of the Liver (EASL) 50th International Liver Congress 2015
April 22 – 26, 2015; Vienna, Austria
Poster Title: Liver-directed allosteric inhibitors of acetyl-CoA carboxylase favorably impact pathophysiology in the progression from NAFLD to NASH and Hepatocellular Carcinoma, including hepatic steatosis, inflammation, and fibrosis Presentation Date and Time: Saturday, April 25, 2015; 3:30 – 4:00 p.m. CET
Poster Viewing: Saturday, April 25, 2015; 4:00 – 6:00 p.m. CET
Poster #LP-30
Note: The full abstract will be made available on the conference website at 7 a.m. CET on the day of the presentation.

About ACC and NASH

Acetyl CoA Carboxylase (ACC), a master regulator of fatty acid synthesis and oxidation, has been a sought-after, yet intractable target over the past two decades. Successful inhibition of ACC may enable new strategies to reduce lipids, inflammation, fibrosis, blood glucose, weight and cardiovascular risk. Nimbus is the first company to successfully design drug-quality allosteric inhibitors targeting ACC for the treatment of metabolic disease as well as cancer.

The company's first indication for ACC-focused clinical development in metabolic disease is Non-alcoholic Steatohepatitis, or NASH, a serious condition that can lead to liver cirrhosis, often leading to transplant, and other complications including hepatocellular carcinoma (liver cancer). Currently there are no therapies specifically approved to treat NASH. Other possible metabolic disease indications for ACC inhibition include type 2 diabetes and hypertriglyceridemia.

About Nimbus

Nimbus Therapeutics harnesses the power of computational chemistry to design breakthroughs for the treatment of substantial and underserved human diseases. The company's focus on metabolic diseases, cancer and immune-inflammatory disorders is driven by its selection of well validated targets that have proven intractable to the approaches taken by others in the pharmaceutical and biotechnology industry. Using its unique approach and technological capabilities, Nimbus is rapidly progressing highly selective and potent small molecules through discovery and development. The company's advanced programs include ACC, IRAK4 and Tyk2. Nimbus is headquartered in Cambridge, Massachusetts (USA). To learn more, please visit www.nimbustx.com.