



# NIMBUS

## THERAPEUTICS

### ACC Inhibitors for Potential Diabetes, Nash and Liver Cancer Treatment

**Company presents updated data on unique series of liver-selective ACC inhibitors showing acute and chronic preclinical efficacy, at The Liver Meeting<sup>®</sup>, the 64<sup>th</sup> Annual Meeting of the American Association for the Study of Liver Diseases**

CAMBRIDGE, Mass. – November 4, 2013 – Nimbus Discovery LLC, a biotechnology company discovering novel medicines against exciting but previously inaccessible drug targets, will present preclinical data at The Liver Meeting<sup>®</sup>, the 64<sup>th</sup> Annual Meeting of the American Association for the Study of Liver Diseases (AASLD), that show the company has optimized a unique series of Acetyl Co-A Carboxylase (ACC) allosteric inhibitors that bind to the BC domain of ACC and demonstrate excellent potency, drug-like properties and preclinical efficacy. The novel, internally-developed small molecules, ND-654 and ND-630, demonstrated desirable *in vitro* and *in vivo* efficacy in experimental models of metabolic disease, diabetes and hepatic steatosis. In an iterative design fashion over 16 months, the potency of this family of compounds were improved >1000x utilizing the company's proprietary small molecule computational drug discovery technology, and drug-like properties were optimized to efficiently deliver development candidate quality molecules.

Simultaneous inhibition of both isoforms of ACC decreases fatty acid synthesis and stimulates fatty acid oxidation and has the potential to favorably affect the morbidity and mortality associated with obesity, diabetes, and fatty liver diseases including non-alcoholic steatohepatitis (NASH). Nimbus' ACC inhibitors, including ND-654 and ND-630, are believed to be the first drug-like allosteric inhibitors to bind the biotin carboxylase (BC) domain of ACC with high potency and selectivity.

Key findings of the Nimbus compounds presented at the conference include:

- ND-654

- Liver specific ND-654 has favorable drug-like properties with a 2700:1 liver to muscle exposure
- Proof-of-mechanism: ND-654 acutely inhibits ACC, with virtually no effect on muscle, resulting in focused pharmacological effects on the liver
- Proof-of-concept: ND-654 demonstrated target engagement in the liver and dose dependently decreased fatty acid production in the liver
- ND-630
  - Liver selective ND-630 has favorable drug-like properties with a 100:1 liver to muscle exposure
  - Proof-of-mechanism: ND-630 acutely inhibits ACC, demonstrating efficacy in both liver and muscle by preventing malonyl Co-A production
  - Proof-of-concept: ND-630 demonstrated target engagement in the liver and muscle
  - Dosing of ND-630 in high sucrose fed diet-induced obesity (DIO) rats showed improvement in insulin sensitivity, improvement in hepatic cholesterol and normalization of hepatic triglycerides, dose dependent decrease of plasma triglycerides and FFAs, and decrease in plasma cholesterol

“Within 16 months, Nimbus has become the first company to identify and optimize a broad portfolio of liver directed, small molecule inhibitors of ACC – a previously intractable disease target,” said Rosana Kapeller, M.D., Ph.D., Chief Scientific Officer of Nimbus. “We are now preparing for ND-630 to enter the clinic in 2015 for the treatment of NASH and diabetes, while we continue to progress ND-654 in preclinical models of hepatocellular carcinoma.”

### **About Nimbus**

Nimbus Discovery, a biotechnology company, harnesses cutting-edge computational technologies to uncover breakthroughs in small molecule pharmacology. We focus on medically important and highly sought-after disease targets that have proven inaccessible to traditional industry approaches. Our robust pre-clinical pipeline includes novel agents for the treatment of cancer, metabolic disease and inflammation. Nimbus is organized as a constellation of small, nimble teams of experienced drug-hunters deployed across program-focused subsidiary companies. Each team is freed from conventional barriers to scientific success, chartered to create solutions, and geared for program asset deals with leading pharmaceutical companies. Founded in 2009, Nimbus partnered with Schrödinger to invent and apply a physics-based approach that establishes a new standard for rational drug design. Nimbus is backed by world-class

life science investors, including Atlas Venture, SR One, Lilly Ventures and Bill Gates. The company has been named by FierceBiotech as one of 2013's Fierce 15, designating it as one of the most promising private biotechnology companies in the industry. For more information please visit [www.nimbustx.com](http://www.nimbustx.com).