NIMBUS
THERAPEUTICS

Irak4 Inhibitors for the Treatment of Rheumatic Diseases

Proprietary physics-based drug discovery technology enabled rapid identification of potent and selective drug candidates for previously inaccessible target

CAMBRIDGE, Mass. – November 12, 2012 – Nimbus Discovery LLC, a biotechnology company discovering novel medicines against exciting but previously inaccessible disease targets, will present data today at the American College of Rheumatology (ACR) Annual Scientific Meeting in Washington, D.C., demonstrating robust efficacy and selectivity of their IRAK4-inhibitors in preclinical models of rheumatic and auto-immune diseases. IRAK4, is a kinase protein, well-validated and long sought after as a target for the treatment of such conditions as lupus, rheumatoid arthritis, psoriasis and inflammatory bowel disease. Previous attempts to identify small molecule modulators of IRAK4 have failed, and yet, the Nimbus compounds show good drug-like properties and are candidates for further development with the potential to make a significant positive impact on patients.

More than 100 conditions fall under the category of rheumatic disease and there are approximately 46 million people in the United States living with some form of the disease. Rheumatic diseases affect the joints and bones and cause chronic joint pain, swelling, and stiffness, and some affect other areas of the body, including the heart, kidneys, lungs, and skin. The drugs currently available to treat most of these conditions do not provide a cure but rather limit the symptoms.

Using a physics-based computational approach, Nimbus and their co-founding partner, Schrödinger Inc., uncovered previously unexploited drivers of potency and selectivity. These insights were used to discover, design, synthesize and test the first truly selective small molecule IRAK4 inhibitors. The three Nimbus novel compounds, ND-346, ND-2110 and ND-2158 demonstrated high selectivity against a panel of 334 kinases, and potent *in vitro* inhibition of cytokine production in cells and whole blood. Moreover,

robust *in vivo* efficacy was achieved in collagen-induced arthritis, psoriasis and mono-sodium urate (MSU) gout mouse models.

“Previous attempts to modulate IRAK4 have resulted in poor selectivity and inadequate drug-like properties,” said Rosana Kapeller, M.D., Ph.D., Chief Scientific Officer of Nimbus. “These data validate Nimbus’ computational approach to drug discovery and demonstrate our ability to quickly and efficiently identify high potential drug candidates for a target that has challenged researchers for more than a decade.”

Download the poster presented by Nimbus Discovery at the 2012 American College of Rheumatology (ACR) Annual Scientific Meeting (PDF File)

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 Gates Ventures. For more information please visit www.nimbustx.com.