**PRESS RELEASE**

**December 16, 2015**

# Saniona's partner TRC will initiate a Phase 2 study for NS2359 in cocaine addiction following grant from Dana Foundation

**Saniona, a leading biotech company in the field of ion channels, announces today that the Dana Foundation has awarded the University of Pennsylvania Treatment Research Center (TRC) a grant of USD 250,000 to conduct a Phase 2 clinical trial for NS2359 for treatment of cocaine addiction. TRC expects to initiate the Phase 2 study during the first half of 2016. Today there are no approved drugs to treat cocaine addiction.**

"We are very pleased that the Dana Foundation has decided to support TRC's Phase 2 clinical study. If this Phase 2 trial proves successful, Saniona and TRC will work with the FDA to determine the design of the Phase 3 trials. We hope that these efforts may lead to the first effective treatment option in cocaine addiction," says Jørgen Drejer, CEO of Saniona.

Dana Foundation has awarded a grant of USD 250,000 to TRC for the Phase 2 clinical trial. Following this grant, TRC plans to initiate the Phase 2 study during the first half of 2016. The objective of the study is to demonstrate cocaine abstinence by the end of an 8-week treatment period. Detailed information on study design will be available at www.ClinicalTrials.gov in the near future.

Saniona will provide the drug substance for the trials. Saniona and TRC intend to work with the FDA to determine the design of the Phase 3 trial if the Phase 2 trial is successful.

In June, Saniona granted TRC rights to perform a Phase 2 clinical trial for cocaine addiction and TRC filed an IND based on drug substance from Saniona and a cross-reference to Saniona's existing IND comprising a significant package of preclinical and clinical data.

In July, the FDA approved the IND for cocaine addiction.

"We are eagerly looking forward to test NS2350 for treatment of cocaine addiction. The scientific rational is clear and supported by preclinical and clinical evidence. We believe that NS2359 may be able reduce cocaine craving and blunt the euphoric effects of cocaine without causing euphoria itself. Therefore, NS2350 represents a very promising candidate, which would be the first approved drug to treat cocaine addiction," says Dr. Wade Berrettini, principal investigator at University of Pennsylvania.

"University of Pennsylvania Treatment Research Center, TRC, is world class within clinical trials on drug addiction. The two principal investigators, Dr. Berrettini and Dr. Kampman, are recognized leaders in addiction research. Their professional approach and commitment to this program is inspiring. Following the announcement of the grant of rights in June 2015, they have managed to secure the approval of the IND as well as the funding for the Phase 2 study in very short time," says Jørgen Drejer, CEO of Saniona.

**For more information, please contact**

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## About NS2359

NS2359 is a triple reuptake inhibitor, which blocks the reuptake of dopamine, norepinephrine, and serotonin in a similar manner to cocaine. However, NS2359 dissociates slowly from these transporters and has a long human half-life (up to 10 days) which makes frequent dosing unnecessary. NS2359s pharmacological profile means that it may be able to reduce cocaine withdrawal symptoms, reduce cocaine craving and reduce cocaine-induced euphoria. In preclinical trials, NS2359 has been shown to reduce the reinforcing effects of cocaine and may have effects on cue induced drug craving. Furthermore, human trials with NS2359 have shown that NS2359 has little abuse potential and does not have adverse interactions with cocaine. Thus, NS2359 is a very promising medication for the treatment of cocaine dependence.

## About Dana Foundation

The Dana Foundation is a private philanthropic organization that supports brain research through grants, publications, and educational programs. The Foundation works to achieve its goals through innovative research grants and through public outreach efforts. The Foundation promotes dialogue between researchers and lay audiences; provides validated information about the latest advances in research through its free publications and websites; engages people worldwide through the Alliances and International Brain Awareness Week; and highlights critical information about the brain through its social media. At the core of the Foundation's philosophy is a belief in the importance of scientific inquiry and the engagement of the public in championing brain research. Read more at www.dana.org.

## About the Treatment Research Center at the University of Pennsylvania, TRC

TRC is a clinical outpatient treatment center that is part of the PENN / VA Center for the Studies of Addiction (CSA). TRC has a modern treatment facility with a fully certified clinical laboratory and a state of the art data management unit. The Investigators have been leaders in addiction pharmacotherapy research for over 35 years and highly experienced clinicians and research associates staff the center. TRC has an active recruitment process and network in place for cocaine addiction. The center screen about 250 cocaine dependent patients per year of which about 100 cocaine dependent patients are randomized into research protocols. TRC offers a comprehensive biopsychosocial evaluation in relation to clinical programs comprising a physical exam and ECG, an outpatient medical detoxification stabilization unit, and daily individual and group therapy sessions that are made available to patients eligible for one of the treatment-research studies.

## About Saniona

*Saniona is a research and development company focused on drugs for diseases of the central nervous system, autoimmune diseases, metabolic diseases and treatment of pain. The company has a significant portfolio of potential drug candidates at pre-clinical and clinical stage. The research is focused on ion channels, which makes up a unique protein class that enables and controls the passage of charged ions across cell membranes. Saniona has an ongoing collaboration agreement with Saniona's Boston based spinout Ataxion Inc., which is financed by Atlas Venture Inc. and Biogen Idec Inc. Saniona is based in Copenhagen, Denmark, where it has a research center of high international standard and 18 employees. Saniona is listed at AktieTorget since April 2014 and has about 3,000 shareholders. The company's share is traded under the ticker SANION. Read more at www.saniona.com.*

## Further details about NS2359 and cocaine addiction

### Cocaine addition

Cocaine dependence continues to be a significant public health problem. In 2012, the National Survey on Drug Use and Health revealed that in the US 639,000 persons used cocaine or crack cocaine for the first time, 1.6 million people had used cocaine at least once during the month prior to the survey, and 1.1 million persons were classified as dependent on or abusing cocaine. Cocaine abuse and dependence leads to significant morbidity and mortality. Medical problems associated with cocaine use include an increased risk of HIV, hepatitis, and serious pulmonary and cardiovascular disease[i]. Other problems associated with cocaine use include increased rates of crime, violence, poverty, and family disruption[ii]. The standard treatment for cocaine dependence consists of individual and group psychotherapy and self-help groups. Although progress has been made in developing new psychosocial treatments for cocaine dependence, psychotherapy alone does not provide substantial benefit for many patients[iii]. Dropout rates in outpatient treatment programs are very high[iv]. Even among patients who complete treatment, relapse is common[v]. Thus, medications have been sought to augment psychosocial treatment. Currently, there are no medications approved for the treatment of cocaine dependence.

### Mode of action and rationale for treatment of cocaine addiction

NS2359 is a triple reuptake inhibitor, which blocks the reuptake of dopamine, norepinephrine, and serotonin in a similar manner to cocaine. Compared to cocaine, NS2359 has greater affinities at the three transporters. However, in contrast to cocaine, NS2359 dissociates slowly from all three transporters and it has a very long human half-life (up to 10 days). Therefore, NS2359 has the potential to block binding of cocaine to these transporters and blunt cocaine reward, even with episodic non-compliance. Furthermore, it may be able to blunt cocaine withdrawal symptoms, which have been associated with reduced dopamine and serotonin activity in newly abstinent cocaine dependent patients[vi]. In addition, as a long acting medication with a mechanism of action similar to that of cocaine, NS2359 may be able reduce cocaine craving and blunt the euphoric effects of cocaine without causing euphoria itself.

Effective medications exist for the treatment of nicotine addiction and opioid addiction. These effective medications have the ability to do one or more of three things: 1) reduce drug withdrawal symptoms, 2) reduce drug craving, and 3) reduce the euphoria associated with the abused drug. The pharmacological profile of NS2359 suggest that NS2359 may fulfil all three characteristics for an effective medication for cocaine addiction. NS2359 has the potential to reduce cocaine withdrawal symptoms (characterized by deficient mono-amine transmission in key brain areas); reduce cue-induced drug cravings; and prevent the euphoria induced by cocaine. NS2359 has a unique long human half-life (up to 10 days) which makes frequent dosing unnecessary.

### Preclinical and clinical evidence for treatment of cocaine addiction

In preclinical studies, NS2359 has demonstrated clear efficacy against cocaine craving behavior in cocaine dependent rodents and monkeys. Preclinical studies have shown that NS2359 reduces cocaine self-administration in Rhesus monkeys and substitutes for cocaine in both rat and monkey drug-discrimination.

NS2359 was originally developed under an agreement with NIDA for the treatment of cocaine addiction. NeuroSearch discontinued the agreement with NIDA in relation to the outlicense of NS2359 to

GlaxoSmithKline in 2004. GlaxoSmithKline performed additional non-clinical and clinical studies under the name GSK372475 in order to investigate NS2359's potential as an antidepressant agent and for the treatment of adults with ADHD. NeuroSearch regained the rights to NS2359 from GlaxoSmithKline in 2009 since the Phase 2 studies indicated that NS2359 had no advantage over current treatment for major depression disorders and adult with ADHD. In total NS2359 has been administered to more than 600 individuals as part of eleven Phase 1 studies (5 single dose and 6 repeat-dose studies) and three Phase 2 studies. These studies indicate that the drug is safe and well tolerated in humans for administration up to 10 weeks. These studies provides also promising evidence for using NS2359 as a treatment for cocaine dependence. NS2359 did not cause euphoria in any of the multiple Phase 1 studies or the Phase 2 clinical trials for major depressive disorder[vii] and adult attention deficit disorder[viii]. Furthermore, in a human laboratory drug discrimination study, NS2359 exhibited no abuse liability in comparison with 15 or 30 mg of amphetamine. In a NIDA sponsored Phase 1 human laboratory interaction study, NS2359 was able to reduce the rewarding valence of 20 or 40 mg of cocaine, and it attenuated the cardiovascular effects of IV cocaine.

**Saniona development strategy for NS2359**

Based on NS2359's pharmacological profile and the promising preclinical and clinical studies, the University of Pennsylvania's Treatment Research Center (TRC) intend to perform a clinical proof-of-concept study with NS2359 for treatment of cocaine addiction, where the rationale is very strong, the medical need substantial and the market potential significant. Saniona and TRC intend to apply for additional public funding to continue the development of NS2359 if the trial proves to be successful. Saniona retains the commercial rights to NS2359.

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[i] Restrepo et al, 2009; Shearer et al, 2007; Cook et al, 2008
[ii] Vaughn et al, 2010; Cunningham et al, 2009
[iii] Alterman et al, 1996; Caroll et al, 2004; Kampman et al, 2001
[iv] Kampman et al, 2002
[v] McKay et al, 2010
[vi] Rothman et al, 2008
[vii] Learned et al, 2011
[viii] Wilens et al, 2008