A TOLERIZING APC-TARGETED VACCIBODY VACCINE AMELIORATES DISEASE IN MOUSE MODELS OF EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS AND NON-OBESE DIABETES

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## Introduction

Nykode Therapeutics has developed a platform that targets antigens directly to antigen presenting cells (APCs) using a modular dimeric protein format known as a Vaccibody<sup>TM</sup>.

Here, Vaccibody<sup>TM</sup> vaccines were designed to deliver a tolerogenic response toward disease-associated antigens via specific APC targeting, administered as purified proteins or pDNA, either alone or co-expressed with immune-modulatory proteins (4<sup>th</sup> modules) in a multicistronic plasmid DNA.

The ability of Vaccibody<sup>TM</sup> vaccines to suppress disease development and modulate immune responses in an APC-targeted and antigen-depended manner was tested in the Experimental Autoimmune Encephalomyelitis (EAE) and Non-Obese Diabetic (NOD) mouse models.

#### **EFFECT OF NYKODE VACCINE IN EAE MOUSE MODEL**

➢ Recombinant Vaccibody<sup>™</sup> in MOG(35-55)/CFA + PTX-induced EAE disease in C57BL/6 mice



➢ APC targeting by Vaccibody<sup>™</sup> is required for effective disease protection in the EAE model





therapeutics

#### NYKODE VACCIBODY MODULAR DESIGN



Multiple targeting units for receptors on tolerizing APCs identified and build into exploratory vaccines including natural ligands and other targeting molecules

Auto-antigens known to elicit immunopathological responses identified and build into exploratory vaccines

Anti-inflammatory cytokines or modulators playing key roles in mediating antiinflammatory immune responses build into exploratory vaccines as 4<sup>th</sup> modules

- > Numerous exploratory vaccines build on above modules and evaluated experimentally
- > Nykode's immunotherapy candidates may be delivered through DNA, mRNA, viral vectors or as rec. proteins
- > Vaccibody<sup>™</sup> vaccine is clinically validated: VB10.16 Therapeutic vaccine candidate for HPV16+ cancers with strong clinical data and broad potential

#### **NYKODE: TOLERANCE INDUCTION MOA**

A low dose of Vaccibody<sup>™</sup> prevents EAE with a dose-dependent decrease in diseaseassociated cytokines at peak of disease

IFNγ





Disease prevention in the EAE model can also be achieved by targeting an alternative target on tolerizing APCs



(Treg) activation and expansion.



≻Vaccibody<sup>™</sup> delivers antigen-specific suppression of EAE









#### EFFECT OF NYKODE VACCINE IN NOD MOUSE MODEL

> DNA vaccination with Vaccibody<sup>TM</sup> targeting tolerizing APCs show durable prevention of diabetes in NOD mice

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# CONCLUSION

These data demonstrate the flexibility of the Vaccibody<sup>™</sup> vaccine platform and its ability to deliver potent tolerizing responses in two different models of autoimmune disease.

### NEXT AND ONGOING

In-depth analysis aimed at further dissecting the immunological and molecular mechanisms behind the disease control mediated by Vaccibody<sup>TM</sup> vaccine, including:

- $\succ$  Further evaluate potency and efficacy of later therapeutic delivery of Vaccibody<sup>TM</sup> in the EAE and NOD model
- Immunological mode of action with focus on Tregs
- $\succ$  Assess Vaccibody<sup>TM</sup> potential for inducing bystander suppression

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