Development of an anti-SEMA4D monoclonal antibody for the treatment of Multiple Sclerosis


Abstract

SEMA4D (VX15/2503) is a secreted interleukin 8-like protein that functions as a cell adhesion molecule and a chemoattractant. A Phase I, multicenter, randomized, double-blind, placebo-controlled study of VX15/2503 in patients with Multiple Sclerosis will begin in late 2012. Enrollment is continuing for this trial. VX15/2503 is a humanized anti-SEMA4D IgG4 monoclonal antibody that specifically inhibits the SEMA4D receptor, which is a key mediator of multiple sclerosis.

Introduction

SEMA4D (VX15/2503) is a secreted interleukin 8-like protein that functions as a cell adhesion molecule and a chemoattractant. A Phase I, multicenter, randomized, double-blind, placebo-controlled study of VX15/2503 in patients with Multiple Sclerosis will begin in late 2012. Enrollment is continuing for this trial. VX15/2503 is a humanized anti-SEMA4D IgG4 monoclonal antibody that specifically inhibits the SEMA4D receptor, which is a key mediator of multiple sclerosis.

Generation of anti-mouse SEMA4D Mabs

| Mab 67-2 | Mab 2955 | Summary of performance antibody for restoring BBB disruption in EAE treatment

Mab 67-2 Reduces EAE clinical scores

- **Mab 67-2** was developed to restore BBB integrity in the EAE model. It was found to be effective in reducing BBB leakage and improving survival rates

Mab 67-2 protects against demyelination and microglial activation in EAE

- **Mab 67-2** was found to be effective in reducing BBB leakage and improving survival rates

Summary

We have generated a high affinity mouse antibody, Mab 67-2, that blocks both SEMA4D-P1 and SEMA4D-C2 and efficiently reduces the severity of disease in both EAE and MS disease models.

**VX15/2503** is a humanized antibody derived from Mab 67-2, exhibits specificity and functional characteristics similar to the mouse proligand antibody. VX15/2503 was found to be effective in reducing BBB leakage and improving survival rates in both EAE and MS disease models.