**KINETIC 3: A Randomized, Double-Blind, Placebo-Controlled Trial of Valbenazine (NBI-98854) for Tardive Dyskinesia**

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**ABSTRACT**

Tardive dyskinesia (TD) is a movement disorder that may occur in patients exposed to dopamine receptor blocking agents (DRBAs), such as antipsychotics. There are currently no FDA-approved medications indicated for the treatment of TD. The vesicular monoamine transporter 2 (VMAT2) is a presynaptic protein that regulates monoamine uptake (e.g., dopamine) from the cytoplasm to the synaptic vesicle for storage and release.

Valbenazine (NBI-98854) is a novel, highly selective inhibitor of VMAT2, in phase 3 development for the treatment of TD.

Valbenazine has a favorable PK profile, allowing once-daily dosing with no required dose adjustment.

In an earlier Phase 2 trial (NCT 01769270), once-daily valbenazine demonstrated efficacy in a well-defined population of treated TD patients.

A Phase 3 trial (NCT 02274558) was conducted to evaluate the efficacy, safety and tolerability of 12-month valbenazine (40 mg and 80 mg) treatment in patients with TD.

**METHODS**

**STUDY DESIGN**

KINETIC 3 was a randomized, double-blind, parallel-group, flexible-dose study (Figure 1).

TI-1000 was titrated to a target dose by day 42 to a maximum of 80 mg (NBI-98854) or matching placebo, as per investigator discretion.

Subjects were randomized (1:1:1) to placebo, valbenazine 40 mg, or valbenazine 80 mg.

Laboratory parameters were similar across treatment groups; no clinically relevant changes were observed.

**Efficacy**

The primary efficacy parameter was met in this study:

- AIMS score (point sum) (LS mean change from baseline to Week 6) in NBI-98854 treated patients versus placebo; valbenazine 40 mg (p = 0.0016) and valbenazine 80 mg (p = 0.007) were statistically significant compared to placebo (p = 0.20).

- The remitting stages of the fixed-sequence titration procedure were met, but a trend toward statistical significance was observed in the remitting stage for valbenazine 40 mg (p = 0.08).

- For the AIMS score change by study visit and for the AIMS total score change from baseline to week 6, there were no statistically significant differences between valbenazine 80 mg and placebo (p = 0.35).

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