

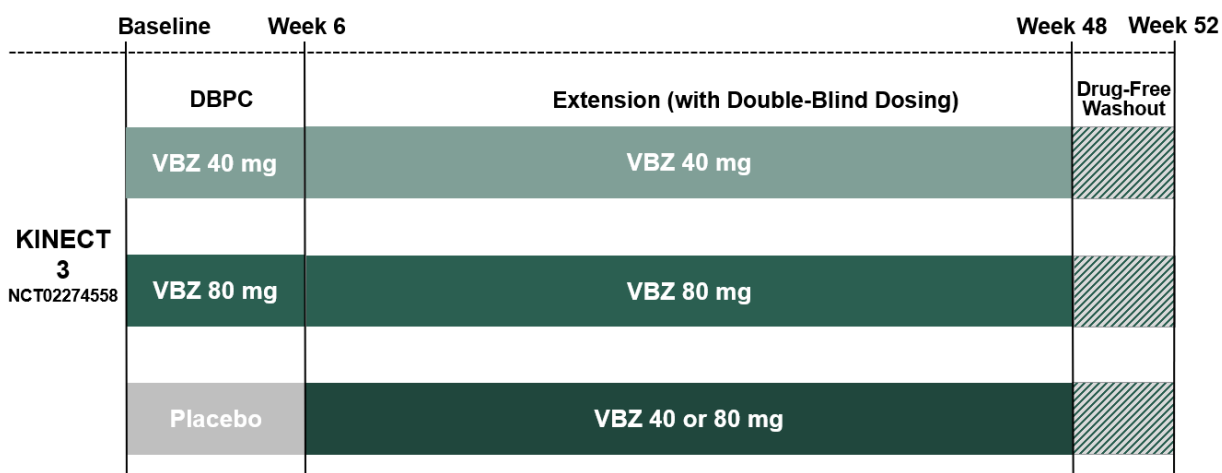
## Long-Term Outcomes in Participants who Achieved Early Improvement with INGREZZA® (valbenazine) capsules

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding long-term outcomes of adult participants with tardive dyskinesia (TD) who achieved early improvement with INGREZZA.

INGREZZA is a vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for the treatment of adults with tardive dyskinesia.<sup>1</sup>

KINECT 3, a randomized, double-blind, placebo-controlled (DBPC) Phase 3 study, was designed to assess the efficacy, safety, and tolerability of valbenazine 40 mg and 80 mg in the treatment of adults with TD. Participants who completed the DBPC period continued with a 42-week double-blind valbenazine extension (VE) period (Week 48) and a 4-week drug-free follow-up period (Week 52) (Figure 1).<sup>2</sup>

**Figure 1. KINECT 3 Study Design<sup>2</sup>**



Participants who were randomized or re-randomized to valbenazine 80 mg were initiated at 40 mg for 1 week; DBPC, double-blind, placebo-controlled; VBZ, valbenazine

Data from the KINECT 3 study were analyzed post hoc to assess the long-term outcomes (as measured by the Abnormal Involuntary Movement Scale, AIMS) of once-daily valbenazine in adult participants with TD who achieved early improvement, based on self-report (Patient Global Impression of Change, PGIC) or clinician judgment (Clinical Global Impression of Change-Tardive Dyskinesia, CGI-TD). Early improvement was defined as those who had a PGIC or CGI-TD score of 1 (“very much improved”), 2 (“much improved”), or 3 (“minimally improved”) at their first post-baseline visit (Week 2) of the DBPC period. Data were analyzed from participants who were initially randomized to valbenazine (40 or 80 mg) and continued receiving valbenazine during the extension phase. Participants who were originally randomized to placebo were not included in this analysis. Long-term outcomes were assessed by a mean change from baseline in the AIMS total score (sum of items 1-7) and an AIMS response ( $\geq 50\%$  total score improvement from baseline) at Week 48, based on scoring by blinded central video raters.<sup>3</sup>

Among participants who received valbenazine (40 or 80 mg) during the KINECT 3 study, 72/143 (50%) achieved early PGIC improvement (score  $\leq 3$  at Week 2), and 61/142 (43%) achieved early CGI-TD improvement (score  $\leq 3$  at Week 2). Baseline demographics and disease characteristics were generally similar between participants who achieved early PGIC or CGI-TD improvement and those who did not.<sup>3</sup>

After 48 weeks of treatment with valbenzazine, mean AIMS total score changes from baseline in participants with early PGIC and CGI-TD improvement were similar to those who did not reach the early improvement thresholds (**Table 1**). Further, AIMS response ( $\geq 50\%$  total score improvement from baseline) at Week 48 were similar in those who achieved early PGIC improvement (all valbenzazine [ $n=14/35$ ], 40%) or CGI-TD improvement (all valbenzazine [ $n=13/31$ ], 42%) compared to those who did not achieve early PGIC improvement (all valbenzazine [ $n=16/41$ ], 39%) or CGI-TD improvement (all valbenzazine [ $n=17/45$ ], 38%).<sup>3</sup>

**Table 1.** AIMS Total Score Mean Change from Baseline to Week 48<sup>3</sup>

Global Improvement at Week 2	Valbenzazine 40 mg		Valbenzazine 80 mg <sup>a</sup>		All Valbenzazine <sup>b</sup>	
	n	Mean Change (SE)	n	Mean Change (SE)	n	Mean Change (SE)
<b>PGIC <math>\leq 3</math></b>	15	-3.7 (1.1)	19	-4.5 (1.1)	35	-4.1 (0.8)
<b>PGIC <math>\geq 4</math></b>	19	-2.5 (1.0)	19	-4.5 (1.0)	41	-3.5 (0.7)
<b>CGI-TD <math>\leq 3</math></b>	13	-4.3 (1.2)	16	-4.3 (1.3)	31	-4.2 (0.8)
<b>CGI-TD <math>\geq 4</math></b>	21	-2.2 (0.9)	22	-4.6 (0.9)	45	-3.5 (0.6)

<sup>a</sup>Includes participants who remained at 80 mg with no dose reductions; <sup>b</sup>Includes participants who had a dose reduction from 80 mg to 40 mg after Week 4; PGIC  $\leq 3$ : "Minimally improved" or better (patient-reported); PGIC  $\geq 4$ : "No change" or worse (patient-reported); CGI-TD  $\leq 3$ : "Minimally improved" or better (clinician-reported); CGI-TD  $\geq 4$ : "No change" or worse (clinician-reported); AIMS, Abnormal Involuntary Movement Scale; CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia; PGIC, Patient Global Impression of Change; SE, standard error.

In the KINECT 3 study, the safety analysis included 227 participants from the three treatment groups, 76 from placebo, 72 from valbenzazine 40mg, and 79 from valbenzazine 80mg. The most commonly reported adverse events ( $\geq 3\%$  of participants in either valbenzazine group at an incidence greater than placebo) for the valbenzazine 40 mg, 80 mg, and placebo groups, respectively, were dry mouth (1.3% vs. 6.9% vs. 0%), somnolence (3.9% vs. 5.6% vs. 5.1%), akathisia (1.3% vs. 4.2% vs. 2.5%), urinary tract infection (3.9% vs. 4.2% vs. 0%), arthralgia (1.3% vs. 1.4% vs. 3.8%), vomiting (0% vs. 0% vs. 3.8%), and dyskinesia (0% vs. 0% vs. 3.8%). There were no treatment-related serious adverse events and no safety signals observed from clinical hematology, chemistry, or ECG readings.<sup>2</sup>

**This letter and the enclosed material are provided in response to your unsolicited medical information inquiry. Please feel free to contact Neurocrine Medical Information at (877) 641-3461 or [medinfo@neurocrine.com](mailto:medinfo@neurocrine.com) if you would like to request additional information.**

**References:**

1. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
2. Hauser RA, et al. KINECT 3: a phase 3 randomized, double-blind, placebo-controlled trial of valbenzazine for tardive dyskinesia. *American Journal of Psychiatry*. 2017; 174:5,476-484.
3. Factor SA, et al. Long-term outcomes in patients with tardive dyskinesia who were early responders with valbenzazine. Poster presented at the International Congress of Parkinson's Disease and Movement Disorders; September 22-26, 2019; Nice, France.

**Enclosure:**

- A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.

- B. Factor SA, et al. Long-term outcomes in patients with tardive dyskinesia who were early responders with valbenazine. Poster presented at the International Congress of Parkinson's Disease and Movement Disorders; September 22-26, 2019; Nice, France.