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Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding INGREZZA® (valbenazine) capsules and data from the KINECT 4 study.

INGREZZA is a vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for the treatment of adults with tardive dyskinesia (TD).[1]

KINECT 4 (NCT02405091) is an open-label, long-term (48-week open-label treatment period and a 4-week drug-free follow-up period) phase 3 study to evaluate the safety and tolerability of valbenazine in adults with TD. Subjects were included in the study if they had a clinical diagnosis of schizophrenia/schizoaffective or mood disorder as defined in the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV). Subjects received a starting dose of once-daily valbenazine 40 mg, which was escalated to 80 mg at the end of Week 4 if both of the following criteria were met: Clinical Global Impression of Change-Tardive Dyskinesia (CGI-TD) score of ≥3 (minimally improved to very much worse) and acceptable safety/tolerability with the 40 mg dose, based on investigator judgment. From Weeks 4 to 48, a decrease to 40 mg was allowed if the subject was unable to tolerate the dose increase (80→40 mg group). Subjects who were unable to tolerate the 40 mg dose were discontinued from the study. Effectiveness was assessed using the Abnormal Involuntary Movement Scale (AIMS) total score (sum of items 1-7), based on consensus scoring by 2 blinded central AIMS video raters (at baseline, Week 8 [first visit after dose escalation] and Week 52 [first visit after treatment withdrawal]) and by the investigator or site rater (at each study visit). Safety assessments included treatment-emergent adverse events (TEAEs).[2]

Of the 163 subjects included in the analyses, 149 subjects reached the Week 8 visit (40 mg, n=33; 80 mg, n=105; 80/40 mg, n=11) and 103 subjects reached the Week 48 visit (i.e., treatment completers; 40 mg, n=20; 80 mg, n=74; 80/40 mg, n=9). Baseline characteristics were similar across treatment groups. Mean baseline AIMS total scores by central video raters were 10.2 (40 mg), 10 (80 mg) and 9.3 (80→40 mg). AIMS results based on central video raters were as follows: mean changes from baseline (CFB) to Week 8 were -4.5 (40 mg), -3.5 (80 mg), and -4.9 (80→40 mg) and mean CFB to Week 52 were -1.8 (40 mg), -3.3 (80 mg), and +0.2 (80→40 mg). AIMS results based on site raters were as follows: mean CFB to Week 8 were -7.5 (40 mg), -5.4 (80 mg), and -7.4 (80→40 mg); mean CFB to Week 48 were -10.2 (40 mg), -11 (80 mg), and -7.2 (80→40 mg); and mean CFB to Week 52 were -3.8 (40 mg), -4.6 (80 mg), and -3.3 (80→40 mg). In summary, AIMS results based on investigator rating indicated sustained reductions in AIMS total score and a return toward baseline levels of dyskinesia after treatment withdrawal.[2]

Approximately two-thirds (64.7 %) of subjects reported ≥1 TEAE at any time during valbenazine treatment. One death occurred due to breast cancer (80 mg), judged by the investigator as not related to study drug. Based on the Columbia-Suicide Severity Rating Scale (C-SSRS), 6.7% of all subjects had any suicidal ideation or behavior during the treatment period. From Week 4 to Week 48, the only TEAEs that occurred in ≥5% of all subjects (combined dose groups) were urinary tract infection (8.5%) and headache (5.2%). Changes from baseline in vital signs, ECG parameters, and laboratory test values were generally small and not clinically significant.[2]

For a more complete description of these analyses, please see attached data presentation from the 2017 American College of Neuropsychopharmacology Annual Congress by Marder S R, et. al.

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 if you would like to request additional information.

References

1. INGREZZA [package insert]. Neurocrine Biosciences, Inc., San Diego, CA; 2017.

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2. Marder S R et. al. KINECT 4: A phase 3, one-year, open-label trial of valbenazine in participants with tardive dyskinesia. Poster presented at the 2017 American College of Neuropsychopharmacology Annual Congress, Palm Springs, CA.

Enclosures:

1. INGREZZA [package insert]. Neurocrine Biosciences, Inc., San Diego, CA; 2017.
2. Important Safety Information. Neurocrine Biosciences, Inc., San Diego, CA; 2017.
3. Marder S R et. al. KINECT 4: A phase 3, one-year, open-label trial of valbenazine in participants with tardive dyskinesia. Poster presented at the 2017 American College of Neuropsychopharmacology Annual Congress, Palm Springs, CA.

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