are allowed. Efficacy outcomes, analyzed by study visit, include mean changes from baseline in Unified Huntington's Disease Rating Scale (UHDRS®) Total Maximal Chorea (TMC) score and response status for Clinical Global Impression of Change (CGI-C) and Patient Global Impression of Change (PGI-C). Responders are defined as participants with a score ≤2 (rating of "much improved" or better). Efficacy outcomes up to Week 50 (˜1 year) are reported. Treatment-emergent adverse events (TEAEs) are presented for all participants who received ≥1 dose of study drug, regardless of time in study (2 to 104 weeks). All interim outcomes were analyzed descriptively.

Results. Of 127 participants enrolled at the time of analysis, 98 (77.2%) had completed KINECT-HD and 29 (22.8%) were newly enrolled. Of 125 participants who received treatment, 65 (52.0%) were female and 118 (94.4%) were white; mean age (±SD) was 54.8 (±11.5) years. A mean reduction in TMC score was observed by Week 2 with valbenazine 40 mg (-3.4 [±3.1], n=118); mean reductions were sustained from Week 8 (5.6 [±3.6], n=110) to Week 50 (-5.8 [±4.1], n=66) (all valbenazine doses). At Week 50, 76.9% (50/65) of participants met the pre-defined threshold for CGI-C response; 74.2% (49/66) met the threshold for PGI-C response. Analyses in participants taking concomitant antipsychotic medications are ongoing and will be presented at the meeting. Of the 125 participants who received treatment, 119 (95.2%) reported at least 1 TEAE and 17 (13.6%) discontinued due to a TEAE. The most commonly reported TEAEs were falls (30.4%), fatigue (24.0%), and somnolence (24.0%).

Conclusions. Interim TMC data from KINECT-HD2 indicated chorea improvement with once-daily valbenazine by Week 2 (3.4 [±3.1] with 40 mg), similar to KINECT-HD Week 2 results (-2.9 [±3.0]). The interim analyses also indicated that long-term treatment with valbenazine was well tolerated and provided clinically meaningful improvement in chorea severity for up to ˜1 year.

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Valbenazine Improves Tardive Dyskinesia with or Without Concomitant Antipsychotic Therapy: A Meta-Analysis of Three Long-Term Valbenazine Trials

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Introduction. Valbenazine is a highly selective vesicular monoamine transporter 2 inhibitor indicated for tardive dyskinesia (TD), a persistent and potentially debilitating movement disorder associated with prolonged antipsychotic exposure. Given the paucity of data regarding the course of TD in patients no longer taking antipsychotics, a meta-analysis of 3 long-term valbenazine studies was conducted in subgroups with and without concomitant antipsychotic use at baseline.

Methods. KINECT™-3 (NCT02274558), KINECT™-4 (NCT02405091), and JKINECT (NCT03176771) data were analyzed in study completers taking antipsychotics at baseline (AP+) and those who were not (AP-). The Abnormal Involuntary Movement Scale (AIMS) total score was used to measure TD severity at baseline, Wk48 (end of valbenazine treatment), and Wk52 (4 weeks after valbenazine withdrawal). The meta-analysis implemented a random-effects model that weighted each study based on inverse variance, adjusted for between-study variance.

Results. Of 576 enrolled patients, 336 (58.3%) were study completers and included for analysis: AP+ (n=269); AP- (n=67). Mean baseline AIMS scores ranged from 7.9–14.9 (AP+) and 10.9–14.5 (AP-). Mean changes from baseline in AIMS scores indicated substantial TD improvements with valbenazine at Wk48 (AP+, 6.1; AP-, -6.5) and return towards baseline severity at Wk52 (AP+, -2.1; AP-, -1.4).

Conclusions. Once-daily valbenazine treatment resulted in substantial and sustained TD improvement through Wk48, with no meaningful differences between AP+ and AP- subgroups. The return towards baseline severity after valbenazine withdrawal shows TD is chronic and often irreversible, even in patients no longer taking antipsychotics. Continuous treatment with valbenazine may be warranted irrespective of antipsychotic therapy.

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Correlates of Psychiatric Polypharmacy Among Child and Adolescent Psychiatric Inpatients

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Background. Rates of psychiatric illness among the child and adolescent population have increased over the past several decades. As social and government agencies work to expand access to mental health treatment, more and more children and adolescents are receiving medications for their symptoms. However, many drugs used in this population are not approved for people under the age of 18, and have not been studied in terms of long-term impact on the developing brain. A significant proportion of these patients receive psychiatric polypharmacy, or the prescription of 2 or more psychotropic agents. This rate has increased from about 8% in 1996 to over 40% in 2005. Factors correlated with polypharmacy include older age, male gender, White race, and low socioeconomic status. Polypharmacy can increase the risk of drug-drug interactions, increase morbidity/mortality through cumulative toxicity, and cause decreased medication adherence.

Study Aims: This study aimed to examine psychiatric polypharmacy specifically among psychiatrically hospitalized patients

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in a New York City hospital, and to determine the impact of the COVID-19 pandemic.
Methods. This IRB-approved study reviewed the medical records of 1101 child and adolescent patients that were psychiatrically hospitalized between June 1 2018 and November 30 2021 at Mount Sinai Morningside. Sociodemographic and clinical information was collected and analyzed using SPSS.
Results. In this sample, 29.4% of patients received psychotropic polypharmacy. The polypharmacy group contained a higher percentage of males, White patients, and fewer Asian/South Asian patients. They had on average more hospitalizations, a longer hospitalization period, and were more likely to be diagnosed with an impulsive/behavioral disorder, developmental disorder, or bipolar spectrum disorder. The polypharmacy group were twice as likely to receive medication for agitation while hospitalized. A regression model identified positive predictors of polypharmacy as having a history of violence and a higher number of psychiatric hospitalizations. Negative predictors included non-White race. White patients had the highest average number of medications and Asian/South Asian patients had the lowest. No impact of the COVID-19 pandemic was found.
Conclusion. Psychiatric polypharmacy is extremely common in the child and adolescent population that requires psychiatric hospitalization. Increased behavioral needs, such as episodes of violence, as well as greater illness severity, as indicated by greater number of hospitalizations, may be the driving factors behind polypharmacy. Further investigation is indicated to determine other contributing causal factors and to track long-term consequences of psychiatric polypharmacy.
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Safety and Tolerability of KarXT (Xanomeline Trospium): Pooled Results From the Randomized, Double-Blind, Placebo-Controlled EMERGENT Trials

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Introduction. In prior studies, the dual M_1/M_4 preferring muscarinic receptor agonist xanomeline demonstrated antipsychotic activity in people with schizophrenia and Alzheimer's disease, but its further clinical development was limited primarily by gastrointestinal side effects. KarXT combines xanomeline and the peripherally restricted muscarinic receptor antagonist trospium chloride. KarXT is designed to preserve xanomeline's beneficial central nervous system effects while mitigating adverse events (AEs) due to peripheral muscarinic receptor activation. The efficacy and safety of KarXT in schizophrenia was demonstrated in the 5-week, randomized, double-blind, placebo-controlled EMERGENT-1 (NCT03697252), EMERGENT-2 (NCT04659161), and EMERGENT-3 (NCT04738123) trials.
Methods. The EMERGENT trials enrolled people with a recent worsening of positive symptoms warranting hospitalization, Positive and Negative Syndrome Scale total score ≥80, and Clinical Global Impression–Severity score ≥4. Eligible participants were randomized 1:1 to KarXT or placebo. KarXT dosing (xanomeline/trospium) started at 50 mg/20 mg twice daily (BID) and increased to a maximum of 125 mg/30 mg BID. Safety was assessed by monitoring for spontaneous AEs after administration of the first dose of trial drug until the time of discharge on day 35. Data from the EMERGENT trials were pooled, and all safety analyses were conducted in the safety population, defined as all participants who received ≥1 dose of trial drug.
Results. A total of 683 participants (KarXT, n=340; placebo, n=343) were included in the pooled safety analyses. Across the EMERGENT trials, 51.8% of people in the KarXT group compared with 29.4% in the placebo group reported ≥1 treatment-related AE. The most common treatment-relatedAEs occurring in ≥5% of participants receiving KarXT and at a rate at least twice that observed in the placebo group were nausea (17.1% vs 3.2%), constipation (15.0% vs 5.2%), dyspepsia (11.5% vs 2.3%), vomiting (10.9% vs 0.9%), and dry mouth (5.0% vs 1.5%). The most common treatment-related AEs in the KarXT group were all mild or moderate in severity.
Conclusions. In pooled analyses from the EMERGENT trials, KarXT was generally well tolerated in people with schizophrenia experiencing acute psychosis. These findings, together with the efficacy results showing a clinically meaningful reduction in the symptoms of schizophrenia, support the potential of KarXT to be the first in a new class of antipsychotic medications based on muscarinic receptor agonism and a well-tolerated alternative to currently available antipsychotics.
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S.C.O.P.E. : Schizophrenia Clinical Outcome Scenarios and Patient-Provider Engagement Platform The Interactive Long-Acting Injectable Antipsychotics Selector

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