Bristol Myers Squibb Presents New Long-term Data from the EMERGENT Program Evaluating COBENFY™ (xanomeline and trospium chloride) in Adults with Schizophrenia at Psych Congress 2024

October 31, 2024

Long-term treatment with COBENFY was associated with continued improvements in symptoms of schizophrenia, demonstrating maintenance of effect

COBENFY was generally well tolerated over 52 weeks with a side effect profile consistent with prior trials of COBENFY in schizophrenia

In-trial qualitative interviews found that a majority of participants treated with COBENFY in the long-term EMERGENT-5 trial reported Quality of Life improvements across physical, social, emotional, and role functioning

PRINCETON, N.J.--(BUSINESS WIRE)-- Bristol Myers Squibb (NYSE: BMY) today announced new topline results from the Phase 3 EMERGENT-4 and EMERGENT-5 open-label trials evaluating the long-term efficacy, safety, and tolerability of COBENFY™ (xanomeline and trospium chloride) in adults with schizophrenia over 52 weeks of treatment. Data were presented at the 2024 Psych Congress, taking place from October 29 – November 2, 2024 in Boston, MA.

“The results from our long-term trials further support the differentiated profile of COBENFY and reinforce prior findings of robust and maintained symptom reduction with long-term treatment,” said Alyssa Johnsen, MD, PhD, senior vice president and head of clinical development, Immunology, Cardiovascular and Neuroscience, Bristol Myers Squibb. “We’re pleased to see a compelling safety and tolerability profile associated with long-term COBENFY treatment that is consistent with prior studies. Additionally, we continue to see a lack of weight gain, movement disorders, or metabolic changes with long-term use, reiterating the distinct profile and unique mechanism of action of COBENFY. With COBENFY now available for adults with schizophrenia, we look forward to further understanding the real-world impact of this differentiated treatment option.”

Long-Term Safety and Efficacy of Xanomeline and Trospium Chloride in Schizophrenia: Results From the 52-Week, Open-Label EMERGENT-4 Trial (Poster 65)

EMERGENT-4 was a Phase 3, 52-week, outpatient, open-label extension study evaluating the long-term safety, tolerability, and efficacy of COBENFY in 156 adults with schizophrenia who previously completed the treatment period of one of the Phase 3, five-week, double-blind, placebo-controlled, efficacy and safety studies, EMERGENT-2 or EMERGENT-3.

In the trial, treatment with COBENFY led to continued improvements in symptoms of schizophrenia across all efficacy measures, including the Positive and Negative Syndrome Scale (PANSS) total, Clinical Global Impression-Severity (CGI-S), PANSS positive subscale, and PANSS negative subscale scores, over 52 weeks. Participants who received placebo in the acute trials demonstrated rapid improvement in symptoms once COBENFY was initiated. At four weeks, PANSS total scores were comparable between those who previously received COBENFY or placebo in the acute trials. Improvements in symptoms of schizophrenia continued throughout the 52-week study regardless of whether participants received COBENFY or placebo in the acute trials. At the end of the trial, 69% of participants who completed the study achieved ≥30% improvement in schizophrenia symptoms from acute trial baseline, as measured by the PANSS total score.

Long-term treatment with COBENFY was generally well-tolerated, with no new safety or tolerability issues identified from prior trials of COBENFY. The most common treatment-related treatment-emergent adverse events, or TEAEs, (≥5%) were nausea, vomiting, dyspepsia, dry mouth, and hypertension. The majority were mild to moderate in intensity, did not lead to discontinuation of COBENFY, and resolved with continued treatment. The discontinuation rate due to TEAEs in EMERGENT-4 was 11%.

COBENFY was associated with a mean change in body weight of -1.9 kg (±4.7 kg) when measured from the acute trial baseline at 52 weeks. Additionally, COBENFY was not associated with clinically meaningful changes in mean prolactin levels or on movement disorder scale scores over 52 weeks. There were no reported TEAEs of akathisia or tardive dyskinesia.

Long-Term Safety, Tolerability, and Efficacy of Xanomeline and Trospium Chloride in People with Schizophrenia: Results From the 52-Week, Open-Label EMERGENT-5 Trial (Poster 67)

EMERGENT-5 was a Phase 3, 52-week, outpatient, open-label study evaluating the long-term safety, tolerability, and efficacy of COBENFY in 566 adults in the U.S. with schizophrenia who had stable symptoms on a prior antipsychotic and no prior exposure to COBENFY. The trial enrolled participants with a PANSS total score ≤80 (mean 66.0) and a CGI-S score ≤4 (mean 3.4), who were considered mild to moderately ill.

Treatment with COBENFY led to improvements in symptoms of schizophrenia across all efficacy measures, including the PANSS total, CGI-S, PANSS positive subscale, and PANSS negative subscale scores at 52 weeks, confirming maintenance of effect with long-term treatment. At week 52, 30% of participants had a ≥30% reduction from baseline in the PANSS total score, with an average reduction of -5.5-points from baseline.

Long-term treatment with COBENFY was generally well tolerated, with no new safety or tolerability issues emerging. The most common treatment-related TEAEs, (≥5%) were nausea, vomiting, constipation, dry mouth, diarrhea, dyspepsia, dizziness, hypertension, and somnolence. The majority of TEAEs were mild or moderate in intensity and did not lead to discontinuation of COBENFY. In EMERGENT-5, the discontinuation rate due to TEAEs was 18%.

Treatment with COBENFY was associated with a mean change in body weight of -2.2 kg (± 6.3 kg) from baseline at 52 weeks. Additionally, COBENFY was not associated with clinically meaningful changes in movement disorder scales or hyperprolactinemia.

Participant Reported Insights from EMERGENT-5 In-Trial Interviews (Poster 195 and Poster 196)

In EMERGENT-5, a qualitative interview-based survey was administered to participants to characterize the self-reported patient experience and perceived changes in Quality of Life (QoL) when taking COBENFY. In the qualitative sub study, interviews were conducted at six weeks (T1; N=70) and six months (T2; N=47) after initiating treatment with COBENFY.

At study entry, most participants reported experiencing negative QoL impacts in the four assessed domains, including physical, social, emotional, and role functioning. Most participants described improvements in their QoL in at least one domain within six weeks of COBENFY treatment (86% improved, 13% unchanged, and 1% worsened).

At six weeks, most participants described experiencing a high level of satisfaction with COBENFY as compared to their prior antipsychotic treatment, which was sustained for up to six months of treatment. Participants also perceived improvements in symptoms of schizophrenia and QoL while reporting little burden associated with treatment as important contributors to their satisfaction. At six months, nearly all participants (93%) indicated that they would recommend COBENFY to a friend of family member, and 78% reported that they would continue COBENFY after the trial if given the option.

About Schizophrenia

Schizophrenia is a persistent and often disabling mental illness impacting how a person thinks, feels and behaves. There are three symptom domains of schizophrenia, which include positive symptoms (e.g., hallucinations, delusions, disordered thinking and speech), negative symptoms (e.g., lack of motivation, lack of emotional expression/flat affect, social withdrawal) and cognitive dysfunction (e.g., impaired attention, deficits in memory, concentration and decision-making). The symptoms of schizophrenia can affect all areas of people's lives, making it difficult to maintain employment, live independently and manage relationships. Schizophrenia affects nearly 24 million people worldwide, including 2.8 million people in the United States, and is one of the top 15 leading causes of disability worldwide.

About COBENFY™ (xanomeline and trospium chloride)

COBENFY™ (xanomeline and trospium chloride), formerly KarXT, is an oral medication for the treatment of schizophrenia in adults. COBENFY combines xanomeline, a dual M_1 - and M_4 -preferring muscarinic receptor agonist, with trospium chloride, a muscarinic receptor antagonist that does not appreciably cross the blood-brain barrier, primarily confining its effects to peripheral tissues. While the exact mechanism of action of COBENFY is unknown, its efficacy is thought to be due to the agonist activity of xanomeline at M_1 and M_4 muscarinic acetylcholine receptors in the central nervous system.

INDICATION

COBENFY™ (xanomeline and trospium chloride) is indicated for the treatment of schizophrenia in adults.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

COBENFY is contraindicated in patients with:

- urinary retention
- moderate (Child-Pugh Class B) or severe (Child-Pugh Class C) hepatic impairment
- gastric retention
- history of hypersensitivity to COBENFY or trospium chloride. Angioedema has been reported with COBENFY and trospium chloride.
- untreated narrow-angle glaucoma

WARNINGS AND PRECAUTIONS

Risk of Urinary Retention: COBENFY can cause urinary retention. Geriatric patients and patients with clinically significant bladder outlet obstruction and incomplete bladder emptying (e.g., patients with benign prostatic hyperplasia (BPH), diabetic cystopathy) may be at increased risk of urinary retention.

COBENFY is contraindicated in patients with pre-existing urinary retention and is not recommended in patients with moderate or severe renal impairment.

In patients taking COBENFY, monitor for symptoms of urinary retention, including urinary hesitancy, weak stream, incomplete bladder emptying, and dysuria. Instruct patients to be aware of the risk and promptly report symptoms of urinary retention to their healthcare provider. Urinary retention is a known risk factor for urinary tract infections. In patients with symptoms of urinary retention, consider reducing the dose of COBENFY, discontinuing

COBENFY, or referring patients for urologic evaluation as clinically indicated.

Risk of Use in Patients with Hepatic Impairment: Patients with hepatic impairment have higher systemic exposures of xanomeline, a component of COBENFY, compared to patients with normal hepatic function, which may result in increased incidence of COBENFY-related adverse reactions.

COBENFY is contraindicated in patients with moderate or severe hepatic impairment. COBENFY is not recommended in patients with mild hepatic impairment.

Assess liver enzymes prior to initiating COBENFY and as clinically indicated during treatment.

Risk of Use in Patients with Biliary Disease: In clinical studies with COBENFY, transient increases in liver enzymes with rapid decline occurred, consistent with transient biliary obstruction due to biliary contraction and possible gallstone passage.

COBENFY is not recommended for patients with active biliary disease such as symptomatic gallstones. Assess liver enzymes and bilirubin prior to initiating COBENFY and as clinically indicated during treatment. The occurrence of symptoms such as dyspepsia, nausea, vomiting, or upper abdominal pain should prompt assessment for gallbladder disorders, biliary disorders, and pancreatitis, as clinically indicated.

Discontinue COBENFY in the presence of signs or symptoms of substantial liver injury such as jaundice, pruritus, or alanine aminotransferase levels more than five times the upper limit of normal or five times baseline values.

Decreased Gastrointestinal Motility: COBENFY contains trospium chloride. Trospium chloride, like other antimuscarinic agents, may decrease gastrointestinal motility. Administer COBENFY with caution in patients with gastrointestinal obstructive disorders because of the risk of gastric retention. Use COBENFY with caution in patients with conditions such as ulcerative colitis, intestinal atony, and myasthenia gravis.

Risk of Angioedema: Angioedema of the face, lips, tongue, and/or larynx has been reported with COBENFY and trospium chloride, a component of COBENFY. In one case, angioedema occurred after the first dose of trospium chloride. Angioedema associated with upper airway swelling may be life-threatening. If involvement of the tongue, hypopharynx, or larynx occurs, discontinue COBENFY and initiate appropriate therapy and/or measures necessary to ensure a patent airway. COBENFY is contraindicated in patients with a history of hypersensitivity to trospium chloride.

Risk of Use in Patients with Narrow-angle Glaucoma: Pupillary dilation may occur due to the anticholinergic effects of COBENFY. This may trigger an acute angle closure attack in patients with anatomically narrow angles. In patients known to have anatomically narrow angles, COBENFY should only be used if the potential benefits outweigh the risks and with careful monitoring.

Increases in Heart Rate: COBENFY can increase heart rate. Assess heart rate at baseline and as clinically indicated during treatment with COBENFY.

Anticholinergic Adverse Reactions in Patients with Renal Impairment: Trospium chloride, a component of COBENFY, is substantially excreted by the kidney. COBENFY is not recommended in patients with moderate or severe renal impairment (estimated glomerular filtration rate (eGFR) <60 mL/min). Systemic exposure of trospium chloride is higher in patients with moderate and severe renal impairment. Therefore, anticholinergic adverse reactions (including dry mouth, constipation, dyspepsia, urinary tract infection, and urinary retention) are expected to be greater in patients with moderate and severe renal impairment.

Central Nervous System Effects: Trospium chloride, a component of COBENFY, is associated with anticholinergic central nervous system (CNS) effects. A variety of CNS anticholinergic effects have been reported with trospium chloride, including dizziness, confusion, hallucinations, and somnolence. Monitor patients for signs of anticholinergic CNS effects, particularly after beginning treatment or increasing the dose. Advise patients not to drive or operate heavy machinery until they know how COBENFY affects them. If a patient experiences anticholinergic CNS effects, consider dose reduction or drug discontinuation.

Most Common Adverse Reactions (≥5% and at least twice placebo): nausea, dyspepsia, constipation, vomiting, hypertension, abdominal pain, diarrhea, tachycardia, dizziness, and gastroesophageal reflux disease.

Use in Specific Populations:

- Moderate or Severe Renal Impairment: Not recommended
- Mild Hepatic Impairment: Not recommended

COBENFY (xanomeline and trospium chloride) is available in 50mg/20mg, 100mg/20mg, and 125mg/30mg capsules.

Please see U.S. Full Prescribing Information , including Patient Information .

About Bristol Myers Squibb

Bristol Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol Myers Squibb, visit us at BMS.com or follow us on LinkedIn, X, YouTube, Facebook and Instagram.

Cautionary Statement Regarding Forward-Looking Statements

This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 regarding, among other things, the research, development and commercialization of pharmaceutical products. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements are based on current expectations and projections about

our future financial results, goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond our control and could cause our future financial results, goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. These risks, assumptions, uncertainties and other factors include, among others, that future study results may not be consistent with the results to date and that COBENFY (xanomeline and trospium chloride) may not achieve its primary study endpoints or receive regulatory approval for the indications described in this release in the currently anticipated timeline or at all, any marketing approvals, if granted, may have significant limitations on their use, and, if approved, whether COBENFY for such indications will be commercially successful. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect Bristol Myers Squibb's business and market, particularly those identified in the cautionary statement and risk factors discussion in Bristol Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2023, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, Bristol Myers Squibb undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.

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