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MediMergent Presents Preliminary Results to FDA from its NMSOAP Evaluation of NOACs vs. Warfarin

Rockville, MD – August 12, 2016. Healthcare data integration and analytics company MediMergent LLC has developed a new data collection platform called the **National Medication Safety Outcomes and Adherence Program (NMSOAP)**, that combines Patient Reported Outcomes (PRO) collected in the voice-of-the-patient with physician/provider medical records and prescription data from network pharmacies. The NMSOAP determines longitudinal risk-related profiles on disease management and treatment, medication adherence and persistence, patient safety, clinical outcomes, drug effectiveness, REMs, and comparative effectiveness. On August 5, 2016 the Company presented to senior members of the Center for Drug Evaluation Research (CDER) of the U.S. Food and Drug Administration (FDA), favorable preliminary results from its first real world evaluation using its NMSOAP technology. This NMSOAP evaluation collects data from patients treated with one of four FDA-approved novel oral anticoagulants [Xarelto® (rivaroxaban), Pradaxa® (dabigatran), Eliquis® (apixaban) or Savaysa (edoxaban)] or standard of care Coumadin® (warfarin and generics] for the prevention of atrial fibrillation (AF) related stroke, deep venous thromboembolism, pulmonary embolism, or other physician prescribed uses of oral anticoagulants.

According to Norman Stockbridge, M.D., Ph.D., Director, Division of Cardiovascular and Renal Products for CDER, “The FDA is hopeful that the NMSOAP approach to patient-directed healthcare data will build upon the information it already has from existing systems while helping to leverage near real-time real world evidence to inform FDA decision making,”.

Preliminary NMSOAP data on the use of NOACs versus Warfarin has been acquired in the U.S. across 35 states from 6,174 patients who were taking oral anticoagulants for either on-label or off-label indications. Of these patients, 3,851 were being treated for stroke prevention associated with atrial fibrillation.

- For AF patients, NMSOAP baseline demographic and outcomes data were compared to data presented in a meta-analysis published by Ruff et. al.[1] that included 71,683 participants enrolled in one of four novel oral anticoagulant trials (RE-LY, ROCKET AF, ARISTOTLE, and ENGAGE AF-TIMI 48). The NMSOAP baseline data were similar to the meta-analysis data for age (including % age $\geq$75 yrs), gender, BMI, renal function, diagnosis of diabetes, and the use of aspirin.
- Vital status was confirmed in 94.2% of the 1,445 NMSOAP patients eligible for the 6-month PRO follow-up survey.
- Compared to the analysis of Ruff et. al., the NMSOAP novel oral anticoagulant-warfarin relative risk data reflected similar trends for all-cause mortality (RR = 1.0$\pm$0.1), ischemic cerebrovascular accidents (strokes) or systemic embolic events (RR $\leq$0.81 in favor of novel oral anticoagulants), and gastrointestinal bleeding (RR $\geq$1.25 in favor of warfarin)

"Novel oral anticoagulants have been quite well-characterized with regard to their safety and efficacy profile for the prevention of atrial fibrillation-related strokes," Dr. Stockbridge continued. "Most of the data are the result of phase 3 clinical trials enriched for patients at high risk of atrial fibrillation related complications. The NMSOAP approach appears to be an important opportunity to explore whether data acquired in the real world, using a more patient-centric approach, that is integrated with medical records and pharmacy data can provide additional information to the already existing knowledge base relating to novel oral anticoagulants and other drugs of interest."

The NMSOAP program improves post-marketing tracking of safety; evaluates evolving patterns of real-world medication adherence and persistence; pilots electronic health record-based study enrollment and data collection, and; assesses the effectiveness of post-approval risk mitigation strategies. The initial real world, post-marketing data collected in the NMSOAP novel oral anticoagulant-warfarin evaluation demonstrates that:

- NMSOAP can recruit and retain patients and collect longitudinal data related to safety, outcomes, drug adherence and comparative effectiveness.
- The NMSOAP methodology can collect real world outcomes data consistent with published data from a meta-analysis of four large pivotal phase 3 clinical trials for stroke prevention in patients with atrial fibrillation.
- The three NMSOAP data sources [PROs, medical records and pharmacy data] are complementary and can serve as a foundation for cross-validation.
- The NMSOAP platform can create mutual incentives among providers, pharmacists and patients that support patient retention."

Kenneth Borow, MD, President and Chief Medical Officer of MediMergent stated, "It is imperative that the patient be brought more intimately into a partnership role in his/her own disease management. An important observation from the NMSOAP novel oral anticoagulant-warfarin evaluation was that the PRO data provided real-world, contemporaneous drug adherence and potential clinical outcomes information that is often unknown to the prescribing physician. Also observed was that the pharmacist and the pharmacy database served as important confirmatory data sources for resolution of discrepancies between the PROs and the patients' medical records."

About the NMSOAP

Established under a Research Collaboration Agreement with CDER, the NMSOAP is a partnership among patients, providers, pharmacists, payers, biopharma companies and regulators designed to collect near real-time real data directly from patients. NMSOAP enrolls patients primarily through pharmacies. As a part of the NMSOAP, the American Pharmacists Association (APhA) has developed a national training program for pharmacists and their staff to aid in collecting PRO data into the NMSOAP database. National retailer Kroger Co., the lead pharmacy chain for the NOAC-warfarin study, has leveraged its network of over 7,000 pharmacists in over 2,000 pharmacies nationwide to enroll patients into NMSOAP. Additional pharmacy partners include SuperValu, The Medicine Shoppe, and Cardinal Health.

1. Ruff CT, et. al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomized trials. Lancet 2014; 383: 955–962