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Positive Phase II Study Data Suggest ARAKODA® (tafenoquine) Numerically Improved Clinical Recovery in Patients with Mild-Moderate COVID-19 Disease

- Recently unblinded clinical trial data suggest that tafenoquine exhibits a therapeutic signal in mild-moderate COVID-19 disease. The drug increased the proportion of clinically recovered patients by between 9 percent (intent to treat population) and 14 percent (per protocol population); the drug decreased the proportion of clinically unrecovered patients by between 27 percent (intent to treat population) and 47 percent (per protocol population), but was underpowered to show statistical significance for the primary endpoint due to early termination of the study at n=86 patients.
- The double-blind, randomized, placebo-controlled Phase II study was designed to evaluate whether administration of 8 x 100 mg tablets of tafenoquine within 168 hours of mild-moderate COVID-19 symptom onset as a 200 mg dose once per day on Days 1, 2, 3 and 10, in accordance with U.S. Food and Drug Administration prescribing information for malaria prophylaxis, could increase the proportion of COVID-19 patients clinically recovered on Day 14 from 70 percent to 85 percent (i.e. a reduction in the proportion of unrecovered patients of 50 percent).

WASHINGTON, D.C. — Preliminary results of a phase II study of ARAKODA® (tafenoquine) for treatment of mild-moderate COVID-19 disease demonstrate a numerical reduction in the proportion of patients not recovered on Day 14, and that the incidence of drug-related adverse events was low (8.4 percent) and mild, according to 60 Degrees Pharmaceuticals, LLC (60P), a pharmaceutical company focused on developing new medicines for infectious diseases.

ARAKODA is an anti-malarial indicated for the prophylaxis of malaria in patients aged 18 years of age and older. It has not been approved by the U.S. Food and Drug Administration (FDA) for use in COVID-19 disease, and safety and effectiveness of tafenoquine in this population have not yet been demonstrated.

“In reviewing the data from this study, we are pleased and encouraged to see, as expected, a therapeutic signal associated with tafenoquine,” said Geoffrey Dow, Chief Executive Officer of 60P. “As a next step toward development of a new COVID-19 treatment option, 60P will conduct additional studies to confirm these findings. We are currently seeking qualified financial and commercial partners to engage with us in this exciting effort.”

About the ARAKODA (tafenoquine) COVID-19 Study

The study was randomized, prospective, double-blind, and placebo-controlled, designed to test the hypothesis that 8 x 100 mg tablets of **ARAKODA**, administered within 168 hours of symptom onset as a 200 mg dose once per day Days 1, 2, 3 & 10, and in accordance with FDA prescribing information for malaria prophylaxis, could increase the proportion of COVID-19 patients clinically recovered on Day 14 from 70 percent to 85 percent (i.e. a reduction in the proportion of unrecovered patients of 50 percent). Clinical recovery was defined as cough being mild or absent, respiratory rate < 24 breaths per minute, and absence of fever and shortness of breath.

Secondary and exploratory endpoints included adverse events, incidence of hospitalization and medical follow-up visits, proportion clinically recovered at Day 28, patient-reported COVID-19 disease symptoms at Day 14, viral load, cytokines and antibody levels. Adult volunteers were randomized (~1:1) to receive tafenoquine or placebo and the study's inclusion/exclusions allowed participation of previously vaccinated individuals.

The original design envisaged completion of the study by n=250 subjects to achieve adequate power. After n=86 patients were randomized, a protocol-mandated interim analysis was conducted and a Drug Safety Monitoring Board after reviewing efficacy and adverse event data, recommended completion of the study without modification. For strategic reasons related to a rapidly changing pandemic and competitive environment, 60P elected to terminate the study early and unblind the data from n=86 patients. Early unblinding made the study underpowered to achieve its primary statistical endpoint.

The study found **ARAKODA** numerically decreased the proportion of patients not recovered by 27 percent in the intent to treat population, and by 47 percent in the per protocol population. Because the study was terminated early, it is underpowered to show statistical significance for the primary endpoint. There were drug-related adverse events in 2.4 percent of placebo subjects and 8.7 percent of tafenoquine patients, all of which were mild. There were three hospitalizations for COVID-19 pneumonia, two in the placebo group and one in the tafenoquine group.

About ARAKODA®

Tafenoquine was discovered by Walter Reed Army Institute of Research and the current study was funded by the United States Army Medical & Materiel Development Activity [USAMMDA]. Tafenoquine was approved for malaria prophylaxis in 2018 in the United States as **ARAKODA** (tafenoquine) and in Australia as KODATEF®. Both were commercially launched in 2019 and are currently distributed through pharmaceutical wholesaler networks in each respective country. They are available at retail pharmacies as a prescription-only malaria prevention drug.

It has been shown that tafenoquine inhibits SARS-CoV-2 replication in monkey kidney and human epithelial cells, and pharmacokinetic simulations suggest lung levels at the FDA-approved dose for malaria prevention may exceed the EC90 of the drug. The antiviral target is not definitively known but is suspected to be the main viral protease. These data provided the rationale for conducting the study of **ARAKODA** in mild-moderate COVID-19 patients, for which financial support was provided by the Department of Defense's (DOD) Joint Program Executive

Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO-CBRND), with the goal of fielding a safe, effective treatment against COVID-19 by repurposing the FDA-approved drug.

According to the Centers for Disease Control and Prevention, the long terminal half-life of tafenoquine, which is approximately 16 days, may offer potential advantages in less-frequent dosing for prophylaxis for malaria.

ARAKODA is not suitable for everyone and patients and prescribers should review the **Important Safety Information** below.

ARAKODA (tafenoquine) Important Safety Information

ARAKODA is an antimalarial indicated for the prophylaxis of malaria in patients aged 18 years of age and older.

Contraindications

ARAKODA should not be administered to:

- Glucose-6-phosphate dehydrogenase (G6PD) deficiency or unknown G6PD status
- Breastfeeding by a lactating woman when the infant is found to be G6PD deficient or if G6PD status is unknown
- Patients with a history of psychotic disorders or current psychotic symptoms
- Known hypersensitivity reactions to tafenoquine other 8-aminoquinolines, or any component of **ARAKODA**

Warnings and Precautions

- **Hemolytic Anemia:** G6PD testing must be performed before prescribing **ARAKODA** due to the risk of hemolytic anemia. Monitor patients for signs or symptoms of hemolysis.
- **G6PD Deficiency in Pregnancy or Lactation: ARAKODA** may cause fetal harm when administered to a pregnant woman with a G6PD-deficient fetus. **ARAKODA** is not recommended during pregnancy. A G6PD-deficient infant may be at risk for hemolytic anemia from exposure to **ARAKODA** through breast milk. Check infant's G6PD status before breastfeeding begins.
- **Methemoglobinemia:** Asymptomatic elevations in blood methemoglobin have been observed. Initiate appropriate therapy if signs or symptoms of methemoglobinemia occur.
- **Psychiatric Effects:** Serious psychotic adverse reactions have been observed in patients with a history of psychosis or schizophrenia, at doses different from the approved dose. If psychotic symptoms (hallucinations, delusions, or grossly disorganized thinking or behavior) occur, consider discontinuation of **ARAKODA** therapy and evaluation by a mental health professional as soon as possible.
- **Hypersensitivity Reactions:** Serious hypersensitivity reactions have been observed with administration of **ARAKODA**. If hypersensitivity reactions occur, institute appropriate therapy.

- **Delayed Adverse Reactions:** Due to the long half-life of **ARAKODA**, (approximately 17 days), psychiatric effects, hemolytic anemia, methemoglobinemia, and hypersensitivity reactions may be delayed in onset and/or duration.

Adverse Reactions

The most common adverse reactions (incidence ≥1 percent) were: headache, dizziness, back pain, diarrhea, nausea, vomiting, increased alanine aminotransferase (ALT), motion sickness, insomnia, depression, abnormal dreams, and anxiety.

Drug Interactions

Avoid co-administration with drugs that are substrates of organic cation transporter-2 (OCT2) or multidrug and toxin extrusion (MATE) transporters.

Use in Specific Populations

Lactation: Advise women not to breastfeed a G6PD-deficient infant or infant with unknown G6PD status during treatment and for 3 months after the last dose of **ARAKODA**.

To report SUSPECTED ADVERSE REACTIONS, contact 60 Degrees Pharmaceuticals at 1-888-834-0225 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. **ARAKODA** full prescribing information is here.

About 60 Degrees Pharmaceuticals

60 Degrees Pharmaceuticals (60P), founded in 2010, focuses on developing new medicines for infectious diseases. 60P's mission is supported through in-kind funding from the U.S. Department of Defense. The company also collaborates with prominent research organizations in the U.S. and Australia. 60P is headquartered in Washington D.C., with a subsidiary in Australia. Further information is available on the company's website, www.60degreespharma.com.

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