June 25, 2020

Dear Research Participant (or Name):

You are receiving this letter because you are currently participating in a research study titled Alliance A221504, "**A Randomized, Double-Blind, Placebo-Controlled Pilot Study of an Oral, Selective Peripheral Opioid Receptor Antagonist In Advanced Non-Small Cell Lung Cancer**." We have information about the study that we would like to share with you.

WHY WAS THIS RESEARCH STUDY BEING DONE?

The main purpose of this study is to test the possibility and safety of long-term use of naloxegol. Other purposes include: to see if naloxegol improves health related quality of life, relieves some of the side effects of the opioid pain medications you are taking, and fights off future growth in the cancer that you have, without affecting how opioids control your pain. In this study, you were randomly assigned to receive either naloxegol or placebo.

WHAT HAS HAPPENED?

The trial was opened to patient enrollment in October 2017. Unfortunately, over the course of the past three years, only 48 patients have participated in this trial, and it has been determined that it is unlikely that the trial will reach its planned goal of 204 patients. As a result, this study will stop enrolling new patients on June 30, 2020. This decision was not based on any new information from Alliance A221504 about the effect (good or bad) of the naloxegol treatment.

ASK YOUR DOCTOR.

It is important for you to talk about this with your doctor.

After discussion of options with your study doctor, if you wish to continue to receive study drug as a medical/clinical intervention on this study, the study drug will continue to be supplied free-of-charge until 6 months after you started treatment. You would also continue the study-specified schedule for visits and monitoring.

Any further treatment will be a decision made between you and your doctor. Regardless of the treatment option that you choose, we would like to continue to collect information about your progress so that we may gather as much valuable information as possible from this study including the impact on health-related quality of life. This information will continue to help us understand and treat this condition. As with any research study, you may always decide to stop participating at any time by informing your study doctor of your choice.

Once you complete at least 6 months of treatment on the study, you will have the option of finding out whether you received naloxegol or placebo. If you choose to find out what you were receiving at the end of 6 months of treatment or later, you will have the option of continuing up to a total of 12 months of treatment if you were receiving naloxegol. If you have already received at least 12 months of study treatment, no additional study drug will be provided after this time point.

You have been a very important part of this study, and we wish to thank you for participating. We will use information learned from this trial to develop other studies and approaches to improve the lives of individuals living with advanced lung cancer. We greatly appreciate your

participation in A221504. Only through volunteers like yourself can we continue to improve cancer treatment.