CLINICAL TRIAL RESULTS

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medicine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer, Inc.

Medicine(s) Studied: PF-05221304

PF-06865571

Protocol Number: C3711001

Dates of Trial: 04 January 2019 to 11 October 2019

Title of this Trial: A study to test whether PF-05221304 and PF-06865571 caused any medical problems and if they were able to lower levels of liver fat when taken alone or together by patients with Non-Alcoholic Fatty Liver Disease (NAFLD)

[A Phase 2a, Randomized, Double Blind (Sponsor-Open), Placebo Controlled, Parallel Group Study to Assess the Pharmacodynamics, Safety, and Tolerability of PF-05221304 and PF-06865571 Co-Administered for 6 Weeks in Adults With Non-Alcoholic Fatty Liver Disease (NAFLD)]

Date(s) of this Report: 19 February 2021

– Thank You –

Pfizer, the Sponsor, would like to thank you for your participation in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results, please contact the doctor or staff at your study site.

WHY WAS THIS STUDY DONE?

Increased fat content in the liver can lead to liver damage. Non-alcoholic Fatty Liver Disease (NAFLD) is one condition caused by increased fat content in the liver. A serious type of NAFLD is called non-alcoholic steatohepatitis, or NASH. Patients who have NASH have an increased risk of severe liver damage and death.

Researchers are looking for treatments for patients with NASH because there are none at the moment. Reducing the amount of fat in the liver may help control or slow down the progression of liver damage and help patients with NASH.

PF-05221304 and PF-06865571 are 2 investigational medicines being studied for the treatment of NASH. In other studies, these investigational medicines are being tested separately. The main goal of this study was to find out what effect the investigational medicines had on the amount of fat in the liver in patients with NAFLD when both investigational medicines were taken together.

Researchers also wanted to learn more about the safety of these investigational medicines when taken together. They monitored patients for any medical problems that happened while they were taking PF-05221304 and PF-06865571.

WHAT HAPPENED DURING THE STUDY?

This study compared 4 groups of patients to find out what effect taking PF-05221304 and PF-06865571 together had on fat content in the liver compared to patients taking PF-05221304 alone, PF-06865571 alone, or placebo. A placebo does not have any medicine in it, but it looks just like the study medicine. The study also tested whether taking these investigational medicines alone or together caused any medical problems over a 6 week period.

The study included patients who:

- Were between the ages of 18 and 70 years old,
- Were overweight to obese,
- Had a medical diagnosis of Type 2 diabetes mellitus (T2DM) and were taking no more than 1 diabetes medication by mouth, or
- Had 2 or more of the following medical problems most often linked to an increased risk of heart disease, stroke, and T2DM ("metabolic syndrome"):
    - high blood sugar
    - high blood pressure
    - low levels of "good" cholesterol
    - high triglycerides [TG]
    - waist circumference ≥40 inches (102 cm) for males or ≥35 inches (89 cm) for females,
- Had liver scarring ("fibrosis") and fat build up in cells in the liver ("steatosis") detected by ultrasound ("FibroScan"), and
- Had liver fat ≥8%.

Patients were put into 1 of 4 treatment groups by chance alone. This is known as a "randomized" study. This is done to make the groups more similar. Reducing differences between the groups (like age or the number of men and women), makes the groups more even to compare.

This trial was also "double-blinded". This means that patients and doctors did not know who was given which medicines. This was done to make sure that the trial results were not influenced in any way.

Each patient in the study took 6 pills twice a day by mouth. The pills for each investigational medicine looked exactly the same as the pills for the placebo. This made it so that patients did not know to which study group they were assigned. The pills taken by patients in each study group are shown in the table below.

Study Group	Pills To Be Taken Every 12 Hours	
	PF-05221304	PF-06865571
PF-05221304 Monotherapy	**3 round pills containing 5 mg each of PF-05221304**	**3 oval shaped pills containing placebo**
PF-06865571 Monotherapy	**3 round pills containing placebo**	**3 oval shaped pills containing 100 mg each of PF-06865571**
Combination Therapy	**3 round pills containing 5 mg each of PF-05221304**	**3 oval shaped pills containing 100 mg each of PF-06865571**
Placebo	**3 round pills containing placebo**	**3 oval shaped pills containing placebo**

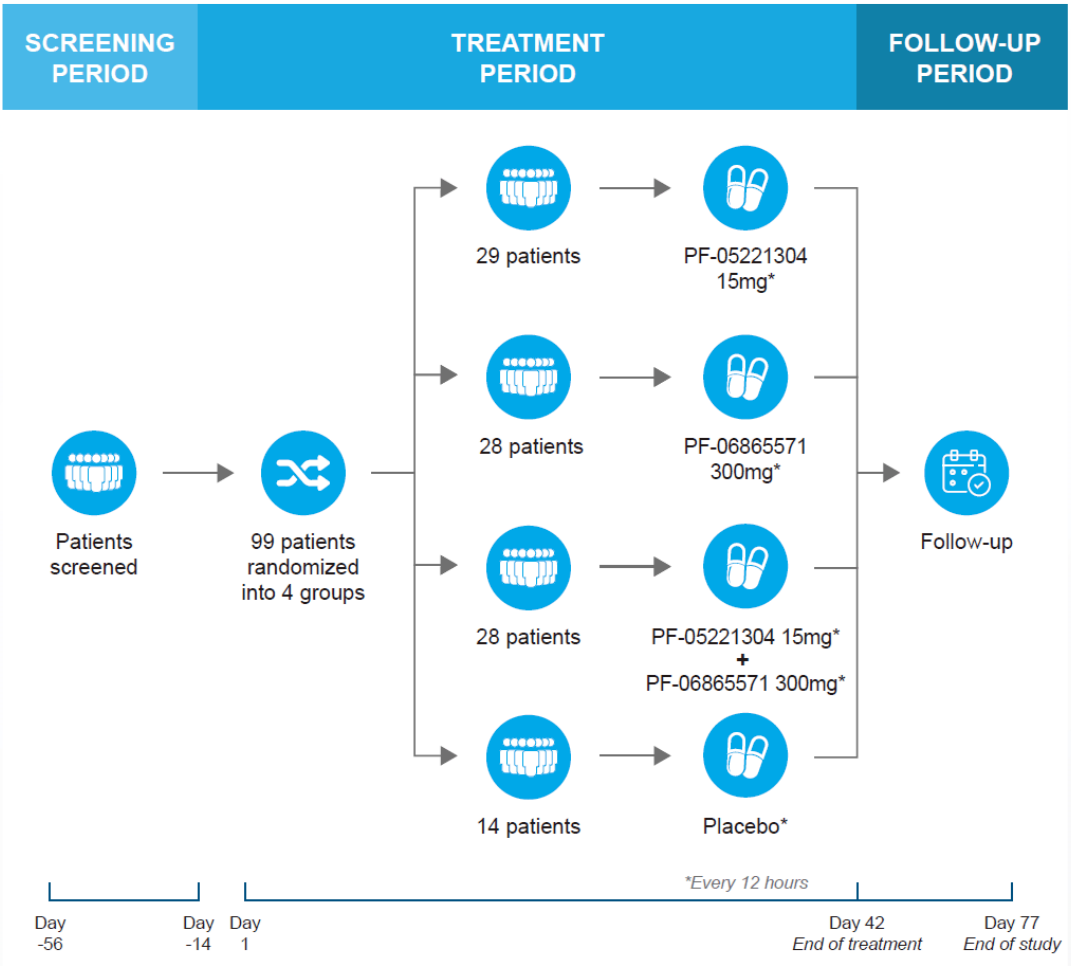
The 4 groups in the study were:

- **PF-05221304 alone:** patients took PF-05221304 and placebo for PF-06865571 (29 out of 99 patients in the study)
- **PF-06865571 alone:** patients took PF-06865571 and placebo for PF-05221304 (28 out of 99 patients in the study)
- **Combination Therapy:** patients took PF-05221304 and PF-06865571 together (28 out of 99 patients in the study)
- **Placebo:** patients took placebo for PF-05221304 and placebo for PF-06865571 (14 out of 99 patients in the study)

The amount of fat in the liver of each patient was measured using a picture called an MRI-PDFF ("magnetic resonance imaging-proton density fat fraction"). This picture was taken at the beginning of the study (Day 1) and at the end of the treatment period (Day 42). The difference in the amount of fat in the liver between Day 1 and Day 42 was determined for each patient. These numbers were combined for all patients in each treatment group and an average change in amount of liver fat was determined

for each of the treatment groups. The average change in the amount of fat in the liver was then compared between treatment groups.

The figure below shows what happened during the study.



While patients were only in the study for up to 19 weeks, the entire study took 9 months to complete. The Sponsor ran this study at 15 locations in the United States. It began 04 January 2019 and ended 11 October 2019. A total of 53 men and 46 women participated. All patients were between the ages of 23 and 71.

Patients were to be treated for 6 weeks. Of the 99 patients who started the study, 83 finished the study. Sixteen (16) patients did not finish the study; of these, 4 patients did not complete the follow-up visits and 12 patients left before the study was over by their choice or a doctor decided it was best for a patient to stop being in the study.

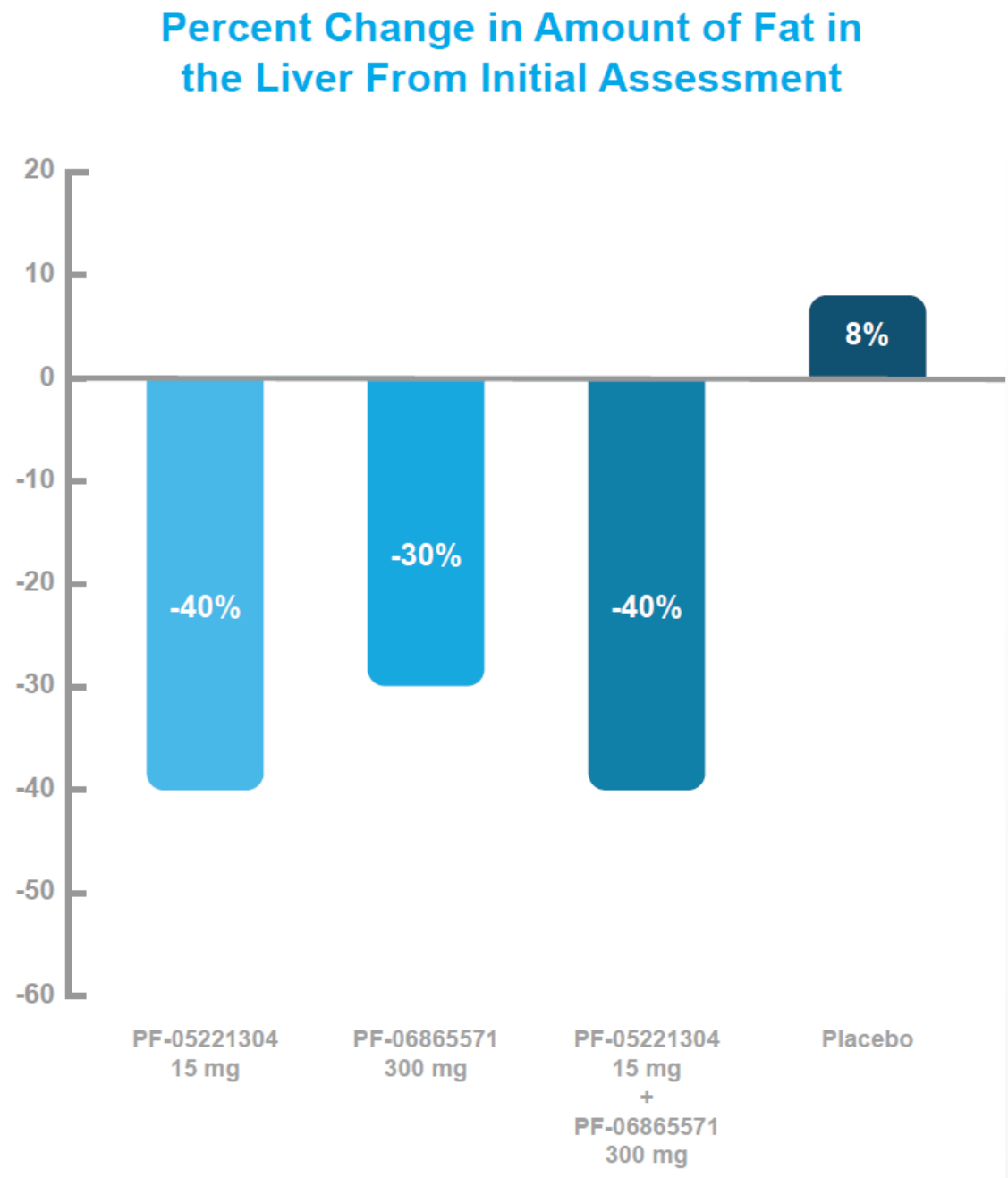
When the study ended in October 2019, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

What effect did taking PF 05221304 and PF 06865571 together have on the amount of fat in the liver compared to taking PF-05221304 alone, PF-06865571 alone, or placebo?

In this study, patients who took both PF-05221304 and PF-06865571 had a decrease in the amount of fat in their liver at the end of the treatment period (Day 42) compared to at the beginning of the study (Day 1). Patients who took either PF-05221304 alone or PF-06865571 alone also had a decrease in the amount of fat in their liver. Patients who took placebo had an increase in the amount of fat in their liver. Over the 6 weeks of the study, liver fat decreased by 40% for patients who took both PF-05221304 and PF-06865571, decreased by 40% for patients who only took PF-05221304, decreased by 30% for patients who only took PF-06865571, and increased by 8% for patients who took placebo.

Based on these results, the researchers have decided that the changes in liver fat recorded during the study are not likely the result of chance. The combination of PF-05221304 and PF-06865571 may be an option for treating patients with NAFLD. In addition, single use of either PF-05221304 or PF-06865571 may also be options for treating patients with NAFLD.



This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

WHAT MEDICAL PROBLEMS DID PARTICIPANTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what the side effects of an experimental drug might be.

A total of 33 out of 99 patients in this study who received at least 1 dose of study medication had at least 1 medical problem. A total of 2 patients left the study because of medical problems. The most common medical problems are listed below.

Most Common Medical Problems (Reported by 2 or More Patients in the Study)				
Medical Problem	PF-05221304 (29 Patients Treated)	PF-06865571 (28 Patients Treated)	PF-05221304 + PF-06865571 (28 Patients Treated)	Placebo (14 Patients Treated)
Urinary tract infection	2 (7%)	0	1 (4%)	0
Diarrhea	1 (3%)	2 (7%)	0	0
Headache	1 (3%)	2 (7%)	0	0
Constipation	1 (3%)	1 (4%)	0	1 (7%)
Increase in blood protein (creatine phosphokinase)	1 (3%)	1 (4%)	0	0
Nausea	1 (3%)	0	1 (4%)	0
Type 2 diabetes mellitus	1 (3%)	0	0	1 (7%)
Rash	0	2 (7%)	0	0
Ear pain	0	1 (4%)	1 (4%)	0
Leg swelling	0	1 (4%)	1 (4%)	0
Nose and throat infection	0	1 (4%)	1 (4%)	0
Abdominal pain	0	1 (4%)	0	1 (7%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.

No patients had serious medical problems. No patients died during the study.

WHERE CAN I LEARN MORE ABOUT THIS STUDY?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

The full scientific report of this study is available online at:

www.clinicaltrials.gov Use the study identifier **NCT03776175**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients. Additional studies with PF-05221304 and PF-06865571 are ongoing.

Again, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!