Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis
Drug Studied: LIK066
Protocol Number: CLIK066B2202

Thank you!

Thank you for taking part in the clinical trial for the trial drug LIK066. You and all of the participants helped researchers learn more about how LIK066 works in people with chronic kidney disease, also called CKD.

Novartis sponsored this trial and believes it is important to share the results of the trial with you and the public. An independent non-profit organization called CISCRP prepared this summary of the trial results for you. We hope it helps you understand your important role in medical research.

If you participated in the trial and have questions about the results, please speak with the doctor or staff at your trial site.

What has happened since the trial ended?

Participants were in this trial for up to about 6 weeks. But, the entire trial took about 8 months to finish. This is because the participants started and stopped at different times. The trial started in April 2017 and ended in January 2018.

The trial included 53 participants from a trial site in the United States. After the trial ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

Why was the research needed?

Before a drug can be approved for patients, researchers do clinical trials to find out about the safety of a drug and how well it works in patients with different diseases. People with CKD have kidneys that do not work properly. The kidneys filter waste, some medicines, and extra water out of the blood to make urine.

LIK066 lowers the body's ability to absorb glucose from the gut and blocks the ability of the kidneys to reabsorb glucose. So when people with normally working kidneys take LIK066, they have glucose in the urine. Having glucose in the urine is a sign that LIK066 is working.

In this trial, the researchers wanted to know how much glucose would be found in the urine of people with CKD who took LIK066 compared to participants who have kidneys that work normally. They also wanted to learn more about the safety of LIK066 in people with CKD.

The main questions the researchers wanted to answer in this trial were:

- Did LIK066 change the amount of glucose in the urine of the participants with CKD?
- How much LIK066 got into the blood of participants with normally working kidneys and participants with CKD?
- What medical problems did the participants have?

What kind of trial was this?

To answer the questions in this trial, the researchers asked for the help of healthy participants and participants with CKD. Some of the participants also had type 2 diabetes. The men and women in this trial were 27 to 78 years old.

This was an "open-label" trial. This means each participant knew what they were taking. The trial staff and sponsor staff also knew what the participant was taking. The sponsor staff did not know the identity of any of the participants.

In this trial, the researchers compared how LIK066 worked in participants with CKD to how it worked in participants whose kidneys worked normally. There was 1 group of participants with kidneys that worked normally and 4 groups of participants with CKD. Each group of participants with CKD was based on how normally their kidneys worked. The more severe the participant's CKD, the less normally the participant's kidneys worked.

There were 4 groups of participants with CKD. These were based on the severity of the CKD, from least to most severe:

- Mild
- Moderate A
- Moderate B
- Severe

What happened during the trial?

Before treatment started, the trial doctors did tests and checked the health of the participants to make sure they could take part in the trial.

The participants began their stay at the trial site 2 days before treatment started. They gave blood and urine samples. All the participants ate the same breakfast the day before treatment started. Giving all the participants the same breakfast helped to make sure that what each participant ate did not affect their results differently.

Participants with CKD joined the trial first. Then, participants with normally working kidneys joined.

During treatment, each participant took LIK066 in pill form once a day before breakfast. The dose of LIK066 was measured in milligrams, also called mg. All participants took 50 mg of LIK066 for 7 days.

The participants stayed at the trial site for all 7 days of trial treatment. During this time, all the participants got the same breakfast after taking LIK066.

After the participants took their first dose of LIK066 on the first day of trial treatment, the trial doctors took blood and urine samples at different times over 24 hours.

Throughout the trial, the trial staff:

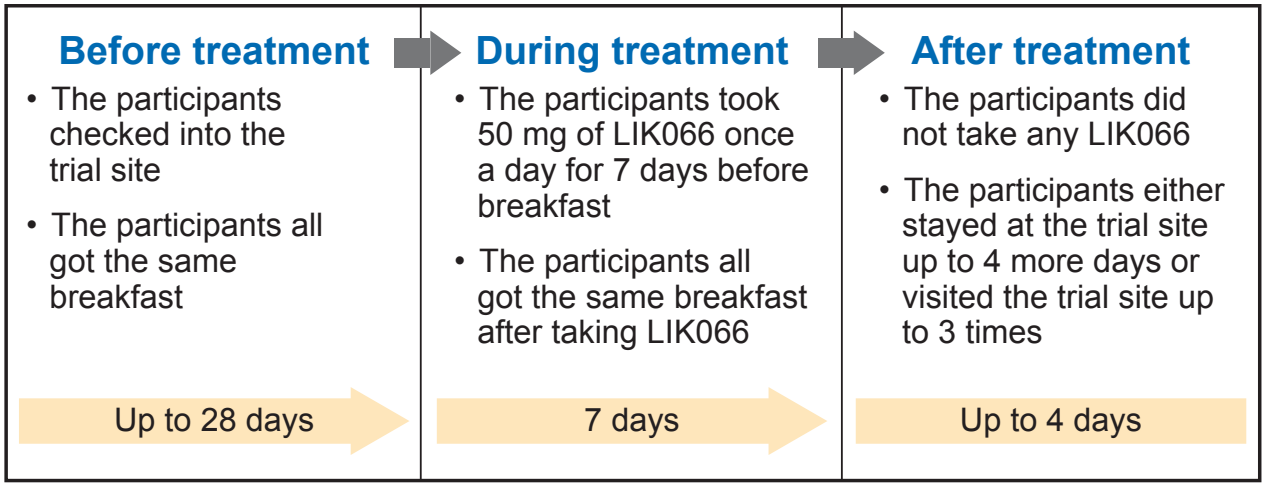
- checked the overall health and heart health of the participants
- took blood and urine samples
- checked how the participants were feeling and what other medications they were taking

After the participants took their last dose of LIK066 on the last day of trial treatment, the trial doctors took more blood and urine samples at different times over 24 hours. Participants with normally working kidneys may have been allowed to leave the trial site the day after the last dose of LIK066.

After treatment, the participants either stayed at the trial site up to 4 days after their last dose or visited the trial site up to 3 more times. At each visit, the trial doctors:

- checked the overall health and heart health of the participants
- took blood and urine samples
- checked how the participants were feeling and what medications they were taking

The chart below shows how the trial was done.



What were the results of the trial?

This is a summary of the overall results of the trial, not your individual results. The results presented here are for a single trial. Other trials may provide new information or different results. You should not make medical decisions based on the results of a single trial. Always talk to a doctor before making any changes to your medications or treatment plans.

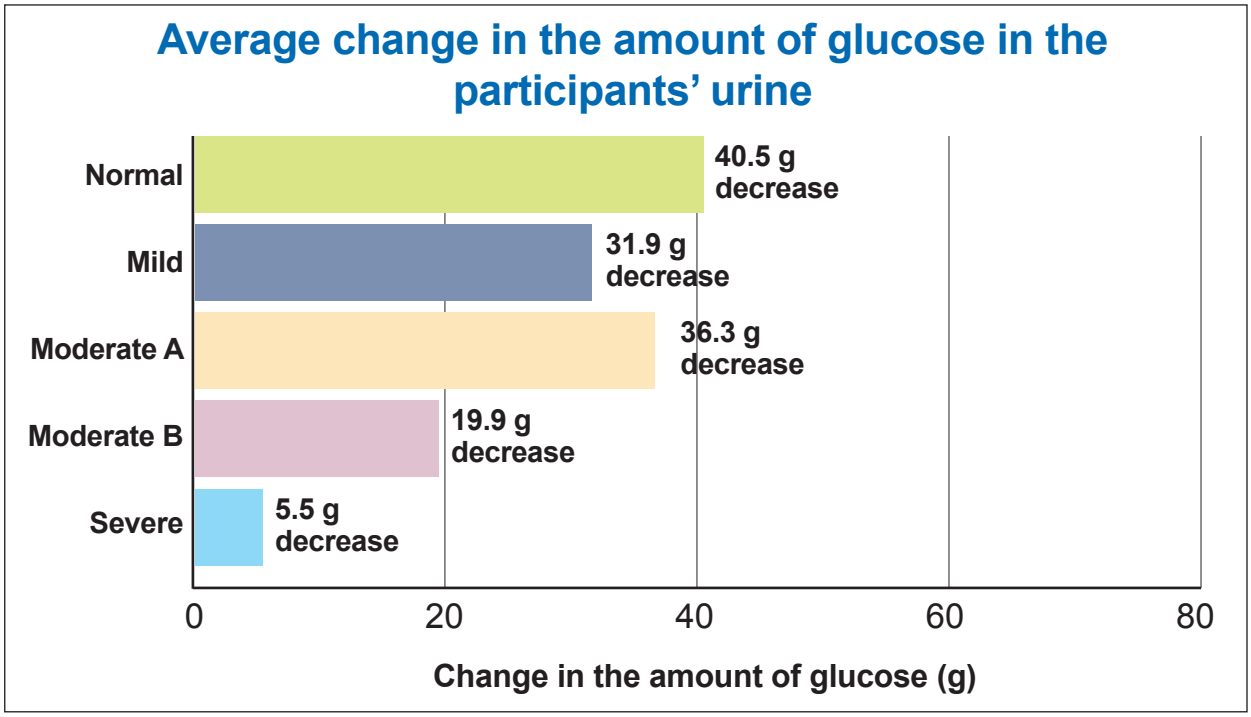
Did LIK066 change the amount of glucose in the urine of the participants with CKD?

Overall, the worse the participants' kidneys worked, the less glucose was found in the participants' urine both before and after treatment with LIK066.

The researchers wanted to know if the participants with CKD had less glucose in their urine after taking LIK066 compared to participants with normally working kidneys. To find out, they measured how much glucose was in the participants' urine after 7 days of trial treatment. They did this by collecting urine samples over 24 hours on the first and last day of trial treatment. This information helped the researchers to better understand if LIK066 could work in people with CKD.

The researchers found that participants in the Moderate B and Severe CKD groups had less glucose in their urine compared to participants with normal working kidneys. They found slight changes in the Mild and Moderate A groups, but these were too small to know if LIK066 caused the changes.

The chart below shows the average change in the amount of glucose in the participants' urine after 7 days of treatment. This amount was measured in grams, also called g.



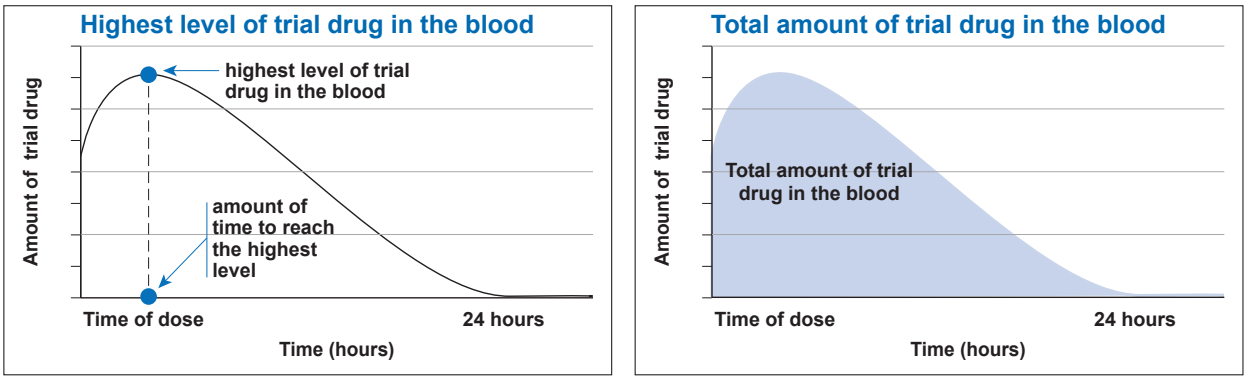
How much LIK066 got into the blood of participants with normally working kidneys and participants with CKD?

Overall, the researchers observed that the average total amount of LIK066 in the participants' blood was higher in participants with kidneys that did not work normally.

To answer this question, the trial doctors measured how much LIK066 was in the participants' blood on the first and last day of treatment. This helped the researchers to find:

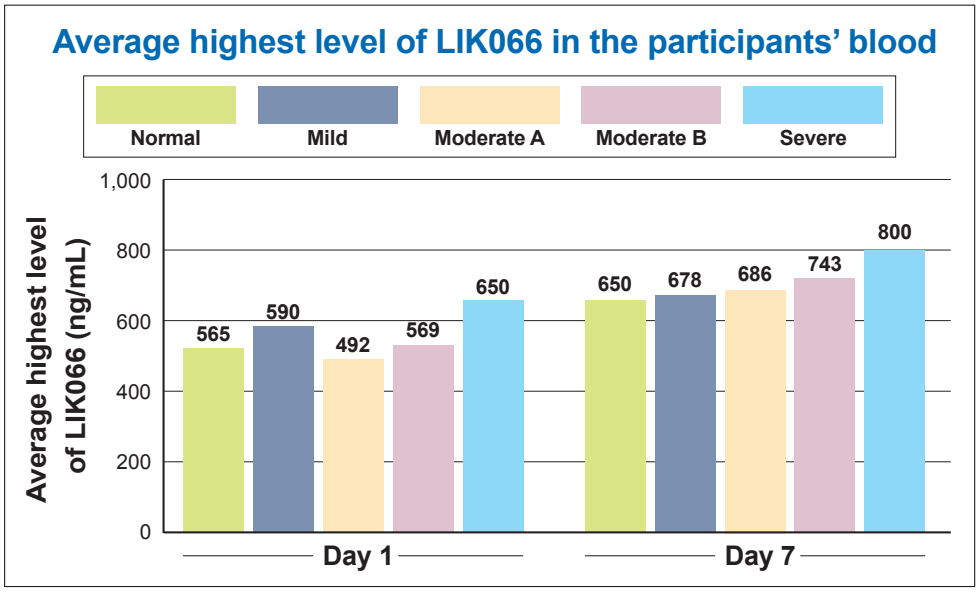
- the average highest level of LIK066 that got into the participants' blood
- the average amount of time it took LIK066 to reach the highest level in the participants' blood
- the average total amount of LIK066 measured in the participants' blood

The graphs below show an example of how the amount of a trial drug in the blood can change over time. They do not show actual results from this trial.

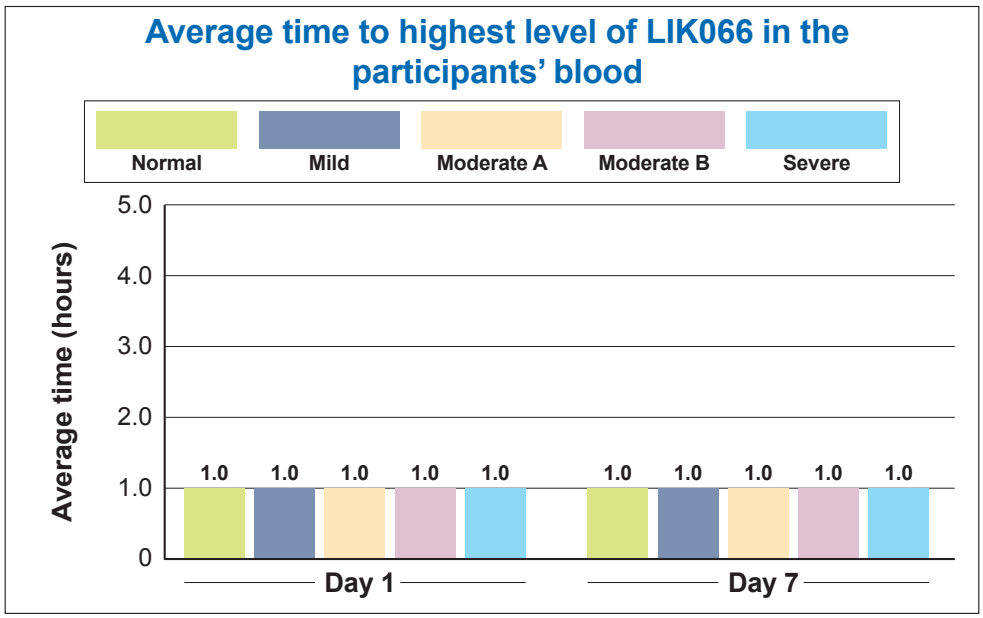


After 7 days of treatment, the researchers found that the less normally the participants' kidneys worked, the more LIK066 was found in the participants' blood.

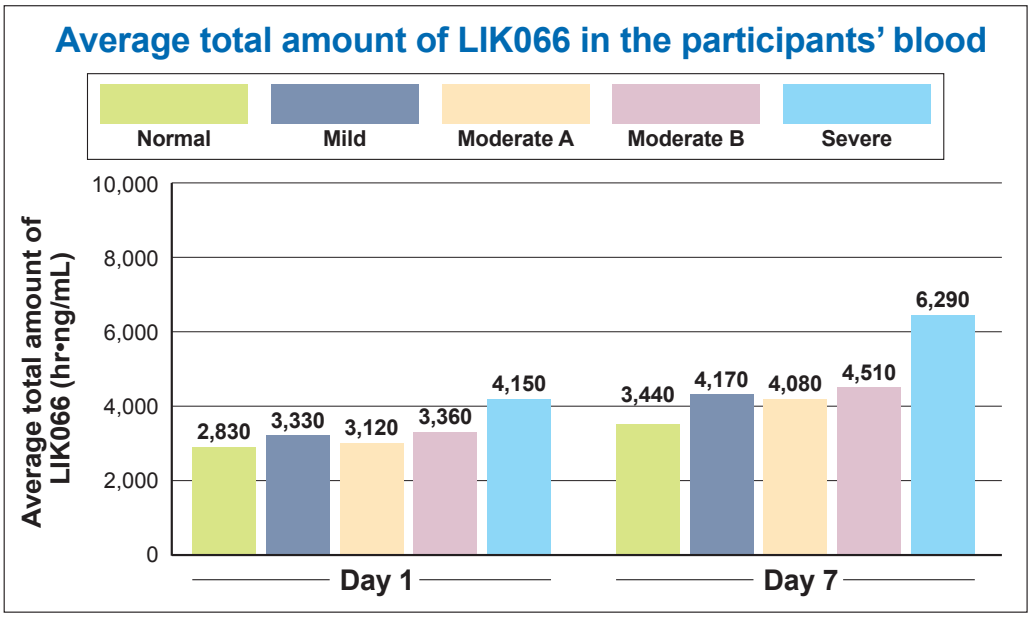
The chart below shows the average highest level of LIK066 in the participants' blood. The researchers measured this on the first day of treatment, Day 1, and on the last day of treatment, Day 7. This was measured in nanograms per milliliter, also called ng/mL.



The chart below shows the average amount of time it took LIK066 to reach the highest level on Day 1 and Day 7. This was measured in hours.



The chart below shows the average total amount of LIK066 in the participants' blood over 24 hours. This was measured on Day 1 and Day 7. This was measured in hours multiplied by nanograms per milliliter, also called hr•ng/mL.



After 7 days, the researchers found that:

- The average total amount of LIK066 was about 29% higher in the participants in the Moderate B CKD group compared to the participants with normally working kidneys.
- The average total amount of LIK066 was about 75% higher in the participants in the Severe CKD group compared to the participants with normally working kidneys.

There were differences between the participants in the Mild or Moderate A CKD groups compared to participants with normally working kidneys. But, these differences were too small for the researchers to know if these differences were due to the severity of the participants' CKD.

The results of 1 participant for Day 7 were not included above because some of the blood samples were taken too late or were not taken.

For more information about measurements of LIK066 in the blood during this trial, please see the scientific summary that can be found on the website noted at the end of this summary.

What medical problems did participants have?

Medical problems that happen in clinical trials are called “adverse events”. An adverse event is any unwanted sign or symptom that participants have during a trial. An adverse event is considered “serious” when it is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug.

A lot of research is needed to know whether a drug causes a medical problem. During a trial, all medical problems are reported and written down, whether or not they are caused by the trial drug. So, when new drugs are being studied, researchers keep track of all medical problems that participants have.

This section is a summary of the adverse events that happened during this trial. All 53 participants are included in these results because they all took at least 1 dose of LIK066.

How many participants had adverse events?

There were a similar number of participants in each treatment group who had adverse events. There was 1 participant each in the Moderate B group and Severe CKD group who had a serious adverse event.

There were 2 participants who stopped taking LIK066 because of an adverse event:

- 1 participant stopped taking LIK066 due to a serious adverse event of the left side of the heart not pumping blood well.
- 1 participant stopped taking LIK066 due to lower than normal blood glucose levels.

The table below shows how many participants had adverse events during this trial.

	Adverse events in this trial					
	Normal (Out of 10 participants)	**Mild (Out of 10 participants)**	**Moderate A (Out of 10 participants)**	**Moderate B (Out of 11 participants)**	**Severe (Out of 12 participants)**	**Total (Out of 53 participants)**
How many participants in this trial had adverse events?	90.0% (9)	100.0% (10)	100.0% (10)	100.0% (11)	91.7% (11)	96.2% (51)
How many participants in this trial had serious adverse events?	0.0% (0)	0.0% (0)	0.0% (0)	9.1% (1)	8.3% (1)	3.8% (2)
How many participants stopped taking LIK066 because of adverse events?	0.0% (0)	0.0% (0)	0.0% (0)	9.1% (1)	8.3% (1)	3.8% (2)

What were the most common serious adverse events?

There were 2 out of 53 participants who had serious adverse events during this trial. This was 3.8% of total participants.

- There was 1 participant who had a serious adverse event of the left side of the heart not pumping blood well. This was 1.9% of total participants. This participant stopped taking LIK066 due to this serious adverse event.
- There was 1 participant who had a serious adverse event of a heart attack. This was 1.9% of total participants.

None of the participants died during this trial.

What were the most common adverse events?

The most common adverse event in this trial was diarrhea. This happened in a similar percentage of participants in all treatment groups. The table below shows the most common adverse events that happened in 2 or more total participants. There were other adverse events, but these happened in fewer participants.

Most common adverse events in this trial

	Normal (Out of 10 participants)	Mild (Out of 10 participants)	Moderate A (Out of 10 participants)	Moderate B (Out of 11 participants)	Severe (Out of 12 participants)	Total (Out of 53 participants)
Diarrhea	90.0% (9)	100.0% (10)	100.0% (10)	90.0% (10)	91.7% (11)	94.3% (50)
Passing gas	70.0% (7)	70.0% (7)	60.0% (6)	81.8% (9)	58.3% (7)	67.9% (36)
Abdominal pain	20.0% (2)	20.0% (2)	10.0% (1)	27.3% (3)	25.0% (3)	20.8% (11)
Nausea	0.0% (0)	10.0% (1)	0.0% (0)	9.1% (1)	8.3% (1)	5.7% (3)
Dizziness	10.0% (1)	0.0% (0)	0.0% (0)	9.1% (1)	0.0% (0)	3.8% (2)
Headache	0.0% (0)	0.0% (0)	0.0% (0)	9.1% (1)	8.3% (1)	3.8% (2)

For more information about the adverse events in this trial, please see the scientific summary that can be found on the websites noted at the end of this summary.

How has this trial helped patients and researchers?

This was the first time that researchers studied LIK066 in people with CKD. The results of this trial helped researchers better understand if LIK066 can work in patients with CKD and to learn more about the safety of LIK066. This summary shows only the main results from this 1 trial. This trial was done in a small number of participants over a short time period. Other trials may provide new information or different results. It takes volunteers in many trials all around the world to advance medical science.

If other trials with LIK066 are planned, you can find them on the websites listed below.

Where can I learn more about this trial?

More information about the results of this trial can be found in the scientific results summary available on the Novartis Clinical Trial Results website (www.novctrd.com). Once on the site, click **"READ MORE"** under **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **"CLIK066B2202"** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the trial doctor or trial staff at your trial site.

You can find more information about this trial on the website listed below:

- www.clinicaltrials.gov. Once you are on the website, type **"NCT03131479"** into the **"Other terms"** search box and click **"Search"**.

If more clinical trials are planned, they will be listed on the above public websites or www.novartisclinicaltrials.com. Search for **"LIK066"**.

Full trial title: An open-label, parallel-group study to assess the effect of LIK066 on urinary glucose excretion, pharmacokinetics, safety and tolerability following multiple dose administration in patients with decreased renal function compared to subjects with normal renal function

Thank you!

As a clinical trial participant, you belong to a large community of participants around the world. You helped researchers answer important health questions and test new medical treatments.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation.

CISCRP
One Liberty Square, Suite 1100
Boston, MA 02109

1-877-MED-HERO • www.ciscrp.org

NOVARTIS

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of participants worldwide.

1-888-669-6682 (US);

+41613241111 (EU)