REZUROCK™
(belumosudil) tablets

When **chronic GVHD** continues to affect your life

ROCK ON WITH REZUROCK

Bringing balance back to your immune system *and keeping you going strong.*

GVHD, graft-versus-host disease.

USE

REZUROCK™ (belumosudil) is a prescription medicine used to treat adults and children 12 years of age and older with chronic graft-versus-host disease (chronic GVHD) after you have received at least 2 prior treatments (systemic therapy) and they did not work. It is not known if REZUROCK is safe and effective in children less than 12 years old.

IMPORTANT SIDE EFFECT INFORMATION

Before taking REZUROCK, tell your healthcare provider about all of your medical conditions, including if you:

- have kidney or liver problems.

Please see additional Important Side Effect Information throughout.
Please see accompanying full Prescribing Information.

Chronic GVHD throws your immune system

OUT OF BALANCE

Learning about chronic GVHD can help you understand what's happening in your body and why. It can also help you make important treatment decisions with your health care team.

Chronic GVHD is a common and serious complication that can happen after a blood stem cell transplant. **IT CAN OCCUR IN HALF OF PEOPLE WHO RECEIVE STEM CELLS FROM A DONOR.**

Chronic GVHD happens most often in people who

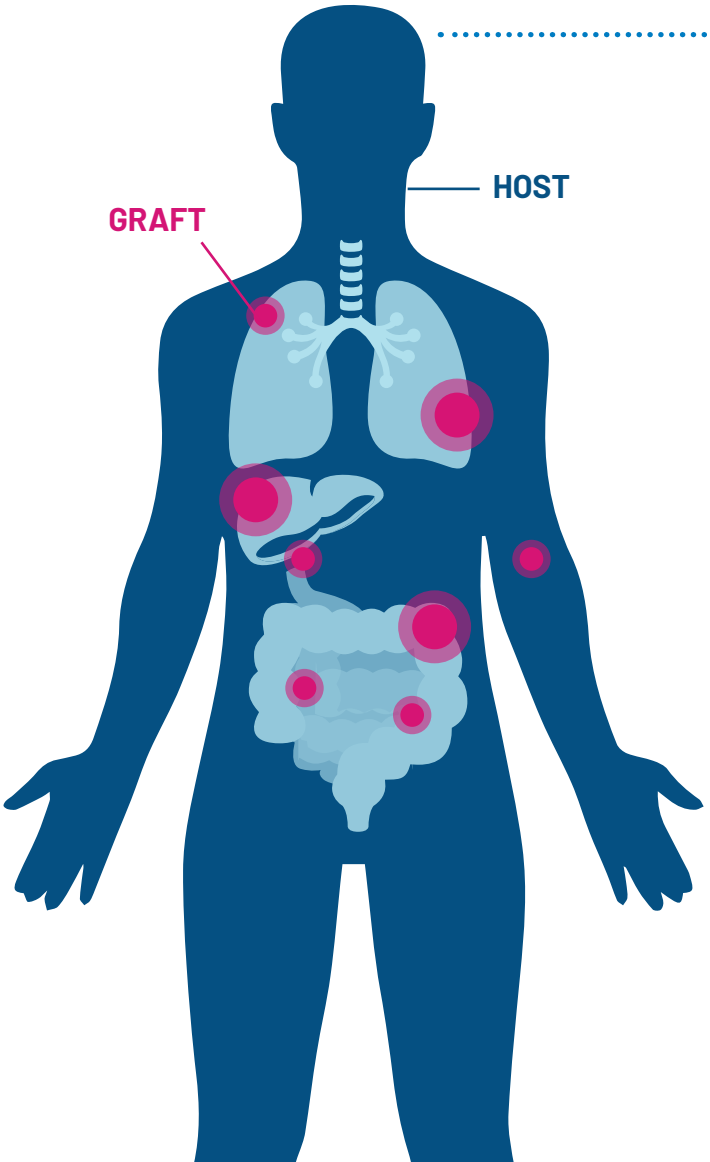
- Received a blood stem cell transplant that was mismatched or unrelated
- Received a transplant with donor cells from the bloodstream rather than donor cells collected from bone marrow or umbilical cord blood
- Had acute GVHD (aGVHD)
- Are male and received cells from a female
- Are older

IMPORTANT SIDE EFFECT INFORMATION (cont)

Before taking REZUROCK, tell your healthcare provider about all of your medical conditions, including if you: (cont)

- are pregnant or plan to become pregnant. REZUROCK can harm your unborn baby. If you are able to become pregnant, your healthcare provider will do a pregnancy test before starting treatment with REZUROCK. Tell your healthcare provider if you become pregnant or think you may be pregnant during treatment with REZUROCK.
  - **Females** who can become pregnant should use effective birth control during treatment with REZUROCK and for at least 1 week after the last dose.

REZUROCK™
(belumosudil) tablets



During a blood stem cell transplant, **stem cells from a donor (the graft)** are added to **your body (the host)**.

DONOR CELLS MAY ATTACK

YOUR BODY'S CELLS AND ORGANS BECAUSE THEY SEE THEM AS A THREAT.

When this happens, it can lead to chronic GVHD. Chronic GVHD causes your immune system to become **UNBALANCED**, creating too many of some cells and not enough of others. This leads to inflammation (swelling) and fibrosis (scarring), which can damage your organs.

IMPORTANT SIDE EFFECT INFORMATION (cont)

Before taking REZUROCK, tell your healthcare provider about all of your medical conditions, including if you: (cont)

- **Males** with female partners who can become pregnant should use effective birth control during treatment with REZUROCK and for at least 1 week after the last dose.

Please see additional Important Side Effect Information throughout.
Please see accompanying full Prescribing Information.

Chronic GVHD is

DIFFERENT FOR EVERYONE

Chronic GVHD can happen at any time after your transplant. It can affect your body and how you feel in many ways, so **IT IS IMPORTANT TO RECOGNIZE SYMPTOMS EARLY** and discuss them with your health care team.

CHRONIC GVHD CAN AFFECT MANY DIFFERENT PARTS OF YOUR BODY

Skin | Eyes | Mouth | Joints and muscles | Stomach and intestines | Liver | Lungs

Common symptoms of chronic GVHD include

- Skin rashes or changes in skin color
- Skin thickening or tightening
- Stiff joints and trouble using your fingers, hands, elbows, knees or ankles
- Dry eyes or vision changes
- Chronic cough, shortness of breath or difficulty breathing
- Nausea, vomiting, diarrhea or loss of appetite
- General decline in health, including fatigue

IMPORTANT SIDE EFFECT INFORMATION (cont)

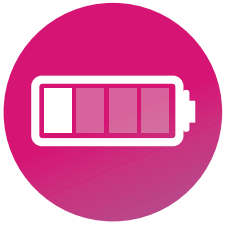
Before taking REZUROCK, tell your healthcare provider about all of your medical conditions, including if you: (cont)

- are breastfeeding or plan to breastfeed. It is not known if REZUROCK passes into breast milk. Do not breastfeed during treatment with REZUROCK and for at least 1 week after the last dose.

REZUROCK™
(belumosudil) tablets

SOME PEOPLE ALSO HAVE

Depression, anxiety



Lack of energy

Reduced ability to do daily tasks

Social interaction problems

Management of chronic GVHD is based on which of your organs are affected, the severity of your symptoms and the impact of the disease on your daily life.

If you have chronic GVHD and are still experiencing symptoms, talk with your health care team about your treatment options.

YOU'RE NOT ALONE.

Visit REZUROCK.com to hear other people with chronic GVHD talk about their condition.

IMPORTANT SIDE EFFECT INFORMATION (cont)

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. REZUROCK may affect the way other medicines work, and other medicines may affect the way REZUROCK works.

Please see additional Important Side Effect Information throughout.
Please see accompanying full Prescribing Information.

REZUROCK

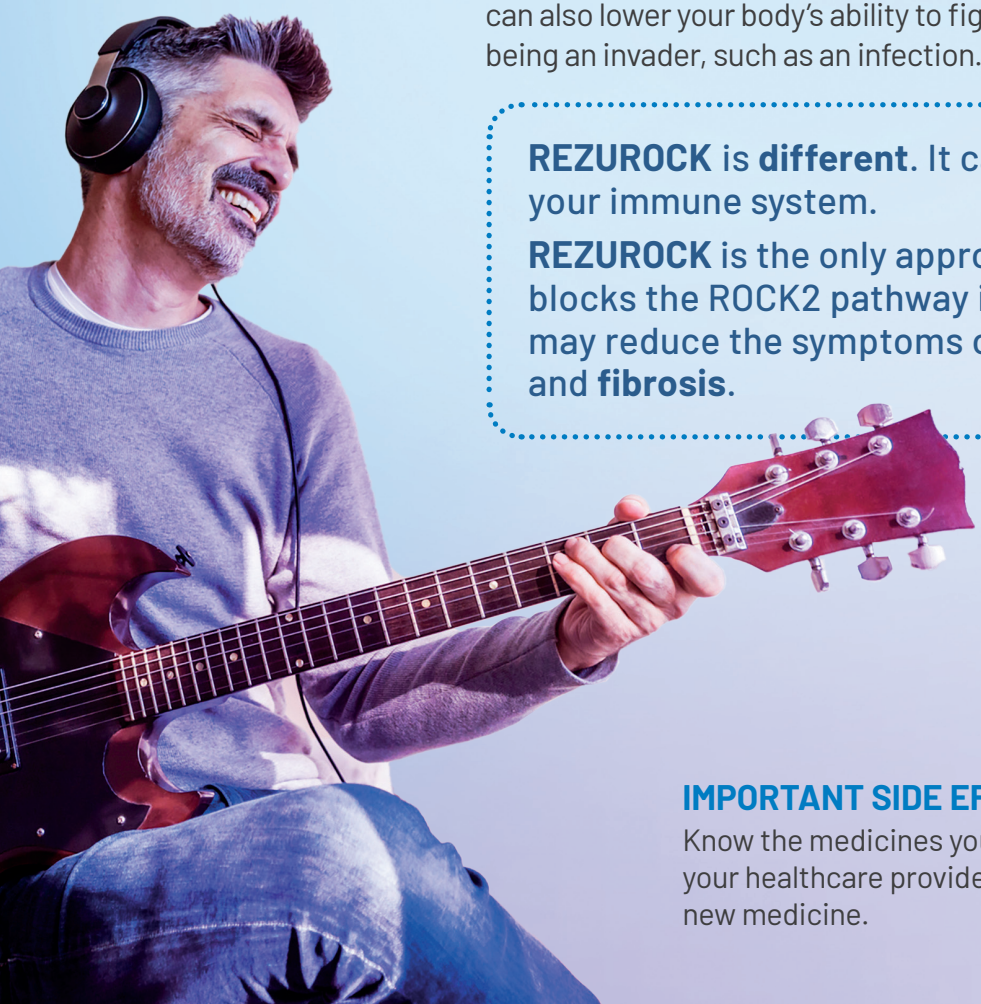
WORKS DIFFERENTLY

Most medicines for chronic GVHD are immunosuppressants (ih-myoo-no-suh-preh-sents)

These medicines suppress (reduce the strength of) your immune system. While these medicines can help treat your condition, they can also lower your body's ability to fight something it recognizes as being an invader, such as an infection.

REZUROCK is **different**. It can help **rebalance** your immune system.

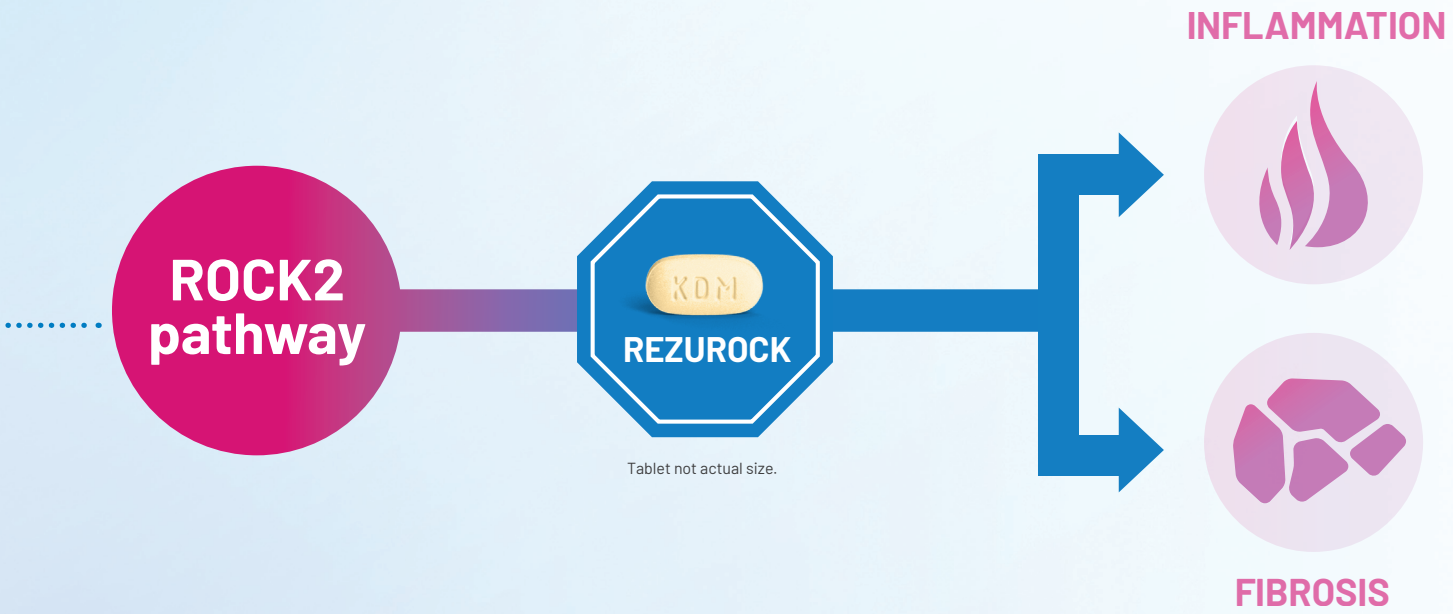
REZUROCK is the only approved medicine that blocks the ROCK2 pathway in your body and may reduce the symptoms of **inflammation** and **fibrosis**.



IMPORTANT SIDE EFFECT INFORMATION (cont)

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

REZUROCK™
(belumosudil) tablets



IMPORTANT SIDE EFFECT INFORMATION (cont)

How should I take REZUROCK?

- Take REZUROCK exactly as your healthcare provider tells you to take it.
- Do not change your dose or stop taking REZUROCK without first talking to your healthcare provider.
- Take REZUROCK 1 time a day with a meal.
- Take REZUROCK at about the same time each day.

Please see additional Important Side Effect Information throughout.
Please see accompanying full Prescribing Information.

HOW REZUROCK CAN HELP YOU...

REZUROCK (belumosudil, bel-you-mos-oo-dill) was evaluated in 2 clinical studies that included a total of 186 people.

Different types of people took REZUROCK in the studies, including

- People who tried immunosuppressants, such as steroids, and other medicines for chronic GVHD that failed to control their symptoms
- People with mild, moderate and severe chronic GVHD
- People with chronic GVHD in 1 or more organs

IMPORTANT SIDE EFFECT INFORMATION (cont)

How should I take REZUROCK? (cont)

- Swallow REZUROCK tablets whole with a glass of water.
- Do not cut, crush, or chew REZUROCK tablets.
- Your healthcare provider will do blood tests to check your liver at least 1 time a month during treatment with REZUROCK.
- If you miss a dose of REZUROCK, take it as soon as you remember on the same day. Take your next dose of REZUROCK at your regular time on the next day. Do not take extra doses of REZUROCK to make up for a missed dose.

ROCK ON

REZUROCK™
(belumosudil) tablets

More than

7 OUT OF 10

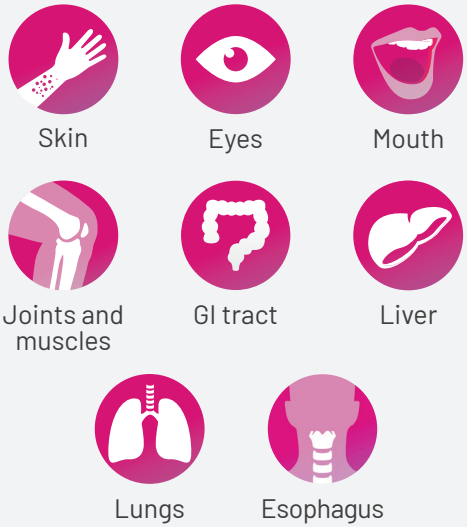
people in the ROCKstar study found symptom relief

Many people found symptom relief within 4 to 8 weeks.

Everyone responds to medicine differently. Some people may take longer to respond, especially if their organs are damaged by scarring.

In some people, REZUROCK reduced the need for steroids and other immunosuppressants.

People saw improvement across multiple organs



REZUROCK also helped improve quality of life for some people, positively impacting both their physical and emotional well-being.

GI, gastrointestinal.

IMPORTANT SIDE EFFECT INFORMATION (cont)

How should I take REZUROCK? (cont)

- If you take too much REZUROCK, call your healthcare provider or go to the nearest hospital emergency room right away.

Please see additional Important Side Effect Information throughout.
Please see accompanying full Prescribing Information.

Why most people were able to

KEEP TAKING REZUROCK

There were **NO NEW CASES** of cytomegalovirus (CMV) infection and only 1 case of recurring CMV infection.

CMV is a common serious infection that can happen in people who have had a blood stem cell transplant.

There was a **LOW RATE OF SERIOUS CYTOPENIA** (site-oh-pee-nia), a condition that causes a lower-than-normal number of certain blood cells.

IMPORTANT SIDE EFFECT INFORMATION (cont)

What are the possible side effects of REZUROCK?
The most common side effects of REZUROCK include:

- infections
- tiredness or weakness
- nausea
- diarrhea
- shortness of breath
- cough
- swelling
- bleeding
- stomach (abdominal) pain
- muscle or bone pain
- headache
- high blood pressure

WHAT SIDE EFFECTS
should I be aware of with REZUROCK?

REZUROCK™
(belumosudil) tablets

The most common side effects reported by people taking REZUROCK in clinical studies were

- Infections
- Tiredness or weakness
- Nausea
- Diarrhea
- Shortness of breath
- Cough
- Swelling
- Bleeding
- Stomach (abdominal) pain
- Muscle or bone pain
- Headache
- High blood pressure

If you have chronic GVHD, staying on your medicine for as long as needed is very important.

Be sure to tell your health care provider about any side effects you have. They may be able to help you find ways to manage them.

Talk with your health care team to find out if REZUROCK is right for you.

IMPORTANT SIDE EFFECT INFORMATION (cont)

What are the possible side effects of REZUROCK? (cont)

Your healthcare provider may change your dose of REZUROCK, temporarily stop, or permanently stop treatment with REZUROCK if you have certain side effects.

Please see additional Important Side Effect Information throughout.
Please see accompanying full Prescribing Information.

How to TAKE REZUROCK

The REZUROCK 200-mg tablet is taken by mouth once a day with a meal

Take REZUROCK at approximately the **SAME TIME EACH DAY WITH A MEAL**.

- A meal is not a snack. It is about the same amount of calories as you might have for lunch or dinner

The REZUROCK tablet should be swallowed whole with a glass of water. **DO NOT CUT, CRUSH OR CHEW THE TABLET.**

If you miss a dose of REZUROCK, take it as soon as you remember on the same day. Take your next dose of REZUROCK at your regular time on the next day. **DO NOT TAKE EXTRA DOSES OF REZUROCK** to make up for a missed dose.

Take REZUROCK as prescribed by your health care team

- Always talk with your health care team about any changes to your medications
- Do not start or stop taking any medicines without discussing it first with your health care team. If you experience a side effect, be sure to tell your health care team right away
- Always let your health care team know about all the medications you are taking

IMPORTANT SIDE EFFECT INFORMATION (cont)

What are the possible side effects of REZUROCK? (cont)

REZUROCK may affect fertility in males and females. Talk to your healthcare provider if this is a concern for you.

REZUROCK™
(belumosudil) tablets

How to store REZUROCK

Store REZUROCK at room temperature, ranging from 68 °F to 77 °F (20 °C–25 °C). REZUROCK should be stored in its original container to protect it from moisture. Make sure to close the cap tightly each time after taking your tablet. Do not discard the drying packet inside the bottle.

Not actual size.

If you are taking REZUROCK, make sure to tell your health care team about all of the prescription and over-the-counter medicines (including proton pump inhibitors, or PPIs), vitamins and herbal products you are taking because they may affect how REZUROCK works.

IMPORTANT SIDE EFFECT INFORMATION (cont)

What are the possible side effects of REZUROCK? (cont)

These are not all the possible side effects of REZUROCK. Call your doctor for medical advice about side effects.

Please see additional Important Side Effect Information throughout.
Please see accompanying full Prescribing Information.

How to GET REZUROCK

Kadmon is committed to helping and supporting people with chronic GVHD, and their caregivers, throughout their treatment journey

Kadmon ASSIST™

Visit **REZUROCK.com,** or call **1-844-KADMON1 (523-6661)**.

Kadmon ASSIST (Access, Support System and Insurance Services for Treatment) is available to help eligible people

- Determine insurance coverage and costs for REZUROCK
- Find a savings program they may qualify for
- Have medicine delivered directly by a specialty pharmacy
- Get answers to their questions from a clinical nurse educator about treatment with REZUROCK

REZUROCK™
(belumosudil) tablets

Learn more about the Kadmon ASSIST support programs designed for people who need treatment for chronic GVHD at **REZUROCK.com**, or call **1-844-KADMON1 (523-6661)**.

Our Kadmon ASSIST team is available to help you **Monday through Friday, 8 AM–8 PM ET**.

Eligible commercially or privately insured people can receive REZUROCK for

AS LITTLE AS $10 PER MONTH

through the Kadmon ASSIST Commercial Co-pay Savings Program.[a]

[a]Patient Terms and Conditions: The Kadmon ASSIST Commercial Co-pay Savings Program provides co-pay/coinsurance support for out-of-pocket costs on REZUROCK™ (belumosudil) tablets prescriptions, up to $25,000 per calendar year, limit one 30-day supply per 30 days. This program is not health insurance. This program is for commercially or privately insured patients only; uninsured or cash-paying patients are not eligible. Patients are not eligible if prescriptions are paid, in whole or in part, by any state- or federally funded programs, including, but not limited to, Medicare (including Part D, even in the coverage gap), or where prohibited by law. Kadmon Pharmaceuticals, LLC, reserves the right to rescind, revoke or amend this offer without further notice. Other limitations may apply.

ROCK ON WITH REZUROCK

- **REZUROCK MAY REDUCE THE SYMPTOMS OF INFLAMMATION AND FIBROSIS** and is the only approved medicine for chronic GVHD that blocks the ROCK2 pathway in the body
- **MORE THAN 7 OUT OF 10 PEOPLE SAW SYMPTOM RELIEF**
- **REZUROCK ALSO REDUCED THE NEED** for steroids and other immunosuppressants in some people
- **REZUROCK HELPED IMPROVE QUALITY OF LIFE** for some people, positively impacting both their physical and emotional well-being
- REZUROCK is a **TABLET**, taken by mouth, that is approved for **ONCE-DAILY DOSING**

Kadmon ASSIST™

Through the Kadmon ASSIST program, we are committed to helping and supporting people with chronic GVHD, and their caregivers, throughout their treatment journey.

Ready to ROCK ON? Ask your health care team if REZUROCK is right for you. For more information about REZUROCK, chronic GVHD and Kadmon ASSIST, visit REZUROCK.com.

IMPORTANT SIDE EFFECT INFORMATION (cont)

You are encouraged to report side effects of prescription drugs to the FDA. Visit **www.FDA.gov/medwatch** or call 1-800-FDA-1088. You may also contact Kadmon Pharmaceuticals, LLC, at 1-877-377-7862 to report side effects.

Please see additional Important Side Effect Information throughout.
Please see accompanying full Prescribing Information.

Kadmon®

KAD25000197 07/21

REZUROCK™
(belumosudil) tablets

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use REZUROCK safely and effectively. See full prescribing information for REZUROCK.

REZUROCK™ (belumosudil) tablets, for oral use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE ----------
REZUROCK is a kinase inhibitor indicated for the treatment of adult and pediatric patients 12 years and older with chronic graft-versus-host disease (chronic GVHD) after failure of at least two prior lines of systemic therapy. (1)

----------DOSAGE AND ADMINISTRATION ----------
Recommended Dosage: 200 mg taken orally once daily with food. (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------
Tablet: 200 mg. (3)

---------- CONTRAINDICATIONS ----------
None. (4)

---------- WARNINGS AND PRECAUTIONS ----------
Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception. (5.1, 8.1, 8.3)

---------- DRUG INTERACTIONS ----------
Strong CYP3A Inducers: Increase REZUROCK dosage to 200 mg twice daily. (7.1)
Proton Pump Inhibitors: Increase REZUROCK dosage to 200 mg twice daily. (7.1)

---------- ADVERSE REACTIONS ----------
The most common (≥ 20%) adverse reactions, including laboratory abnormalities, were infections, asthenia, nausea, diarrhea, dyspnea, cough, edema, hemorrhage, abdominal pain, musculoskeletal pain, headache, phosphate decreased, gamma glutamyl transferase increased, lymphocytes decreased, and hypertension. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Kadmon Pharmaceuticals, LLC at 1-877-377-7862 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- USE IN SPECIFIC POPULATIONS ----------
Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 7/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

REZUROCK is indicated for the treatment of adult and pediatric patients 12 years and older with chronic graft-versus-host disease (chronic GVHD) after failure of at least two prior lines of systemic therapy.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dose of REZUROCK is 200 mg given orally once daily until progression of chronic GVHD that requires new systemic therapy.

Instruct the patient on the following:

- Swallow REZUROCK tablets whole. Do not cut, crush, or chew tablets.
- Take REZUROCK with a meal at approximately the same time each day *[see Clinical Pharmacology (12.3)]*.
- If a dose of REZUROCK is missed, instruct the patient to not take extra doses to make up the missed dose.

Treatment with REZUROCK has not been studied in patients with pre-existing severe renal or hepatic impairment. For patients with pre-existing severe renal or hepatic impairment, consider the risks and potential benefits before initiating treatment with REZUROCK *[see Clinical Pharmacology (12.3)]*.

2.2 Dose Modifications for Adverse Reactions

Monitor total bilirubin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) at least monthly.

Modify the REZUROCK dosage for adverse reactions as per **Table 1**.

Table 1: Recommended Dosage Modifications for REZUROCK for Adverse Reactions

Adverse Reaction	**Severity***	**REZUROCK Dosage Modifications**
Hepatotoxicity *[see Adverse Reactions (6.1)]*	Grade 3 AST or ALT (5x to 20x ULN) or Grade 2 bilirubin (1.5x to 3x ULN)	Hold REZUROCK until recovery of bilirubin, AST and ALT to Grade 0-1, then resume REZUROCK at the recommended dose.
	Grade 4 AST or ALT (more than 20x ULN) or Grade ≥ 3 bilirubin (more than 3x ULN)	Discontinue REZUROCK permanently.
Other adverse reactions *[see Adverse Reactions (6.1)]*	Grade 3	Hold REZUROCK until recovery to Grade 0-1, then resume REZUROCK at the recommended dose level.
	Grade 4	Discontinue REZUROCK permanently.

*Based on CTCAE v 4.03

2.3 Dosage Modification Due to Drug Interactions

Strong CYP3A Inducers

Increase the dosage of REZUROCK to 200 mg twice daily when coadministered with strong CYP3A inducers *[see Drug Interactions (7.1)]*.

Proton Pump Inhibitors

Increase the dosage of REZUROCK to 200 mg twice daily when coadministered with proton pump inhibitors *[see Drug Interactions (7.1)]*.

3 DOSAGE FORMS AND STRENGTHS

Each 200 mg tablet is a pale yellow film-coated oblong tablet debossed with "KDM" on one side and "200" on the other side.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Embryo-Fetal Toxicity

Based on findings in animals and its mechanism of action, REZUROCK can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of belumosudil to pregnant rats and rabbits during the period organogenesis caused adverse developmental outcomes including embryo-fetal mortality and malformations at maternal exposures (AUC) less than those in patients at the recommended dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with REZUROCK and for at least one week after the last dose *[see Use in Specific Populations (8.1, 8.3), Nonclinical Toxicology (13.1)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely variable conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared with rates of clinical trials of another drug and may not reflect the rates observed in practice.

Chronic Graft versus Host Disease

In two clinical trials (Study KD025-213 and Study KD025-208), 83 adult patients with chronic GVHD were treated with REZUROCK 200 mg once daily *[see Clinical Studies (14.1)]*. The median duration of treatment was 9.2 months (range 0.5 to 44.7 months).

Fatal adverse reaction was reported in one patient with severe nausea, vomiting, diarrhea and multi-organ failure.

Permanent discontinuation of REZUROCK due to adverse reactions occurred in 18% of patients. The adverse reactions which resulted in permanent discontinuation of REZUROCK in > 3% of patients included nausea (4%). Adverse reactions leading to dose interruption occurred in 29% of patients. The adverse reactions leading to dose interruption in ≥ 2% were infections (11%), diarrhea (4%), and asthenia, dyspnea, hemorrhage, hypotension, liver function test abnormal, nausea, pyrexia, edema, and renal failure with (2% each).

The most common (≥ 20%) adverse reactions, including laboratory abnormalities, were infections, asthenia, nausea, diarrhea, dyspnea, cough, edema, hemorrhage, abdominal pain, musculoskeletal pain, headache, phosphate decreased, gamma glutamyl transferase increased, lymphocytes decreased, and hypertension.

Table 2 summarizes the nonlaboratory adverse reactions.

Table 2: Nonlaboratory Adverse Reactions in ≥ 10% Patients with Chronic GVHD Treated with REZUROCK

Adverse Reaction	REZUROCK 200 mg once daily (N=83)	
	All Grades (%)	Grades 3-4 (%)
Infections and infestations		
Infection (pathogen not specified)[a]	53	16
Viral infection[b]	19	4
Bacterial infection[c]	16	4
General disorders and administration site conditions		
Asthenia[d]	46	4
Edema[e]	27	1
Pyrexia	18	1
Gastrointestinal		
Nausea[f]	42	4
Diarrhea	35	5
Abdominal pain[g]	22	1
Dysphagia	16	0
Respiratory, thoracic and mediastinal		
Dyspnea[h]	33	5
Cough[i]	30	0
Nasal congestion	12	0
Vascular		
Hemorrhage[j]	23	5
Hypertension	21	7
Musculoskeletal and connective tissue		
Musculoskeletal pain[k]	22	4

Adverse Reaction	REZUROCK 200 mg once daily (N=83)	
	All Grades (%)	Grades 3-4 (%)
Muscle spasm	17	0
Arthralgia	15	2
Nervous system		
Headache[l]	21	0
Metabolism and nutrition		
Decreased appetite	17	1
Skin and subcutaneous		
Rash[m]	12	0
Pruritus[n]	11	0

[a] infection with an unspecified pathogen includes acute sinusitis, device related infection, ear infection, folliculitis, gastroenteritis, gastrointestinal infection, hordeolum, infectious colitis, lung infection, skin infection, tooth infection, urinary tract infection, wound infection, upper respiratory tract infection, pneumonia, conjunctivitis, sinusitis, respiratory tract infection, bronchitis, sepsis, septic shock.

[b] includes influenza, rhinovirus infection, gastroenteritis viral, viral upper respiratory tract infection, bronchitis viral, Epstein-Barr viremia, Epstein-Barr virus infection, parainfluenzae virus infection, Varicella zoster virus infection, viral infection.

[c] includes cellulitis, Helicobacter infection, Staphylococcal bacteremia, catheter site cellulitis, Clostridium difficile colitis, Escherichia urinary tract infection, gastroenteritis Escherichia coli, Pseudomonas infection, urinary tract infection bacterial.

[d] includes fatigue, asthenia, malaise.

[e] includes edema peripheral, generalized edema, face edema, localized edema, edema.

[f] includes nausea, vomiting.

[g] includes abdominal pain, abdominal pain upper, abdominal pain lower.

[h] includes dyspnea, dyspnea exertional, apnea, orthopnea, sleep apnea syndrome.

[i] includes cough, productive cough.

[j] includes contusion, hematoma, epistaxis, increased tendency to bruise, conjunctival hemorrhage, hematochezia, mouth hemorrhage, catheter site hemorrhage, hematuria, hemothorax, purpura.

[k] includes pain in extremity, back pain, flank pain, limb discomfort, musculoskeletal chest pain, neck pain, musculoskeletal pain.

[l] includes headache, migraine.

[m] includes rash, rash maculo-papular, rash erythematous, rash generalized, dermatitis exfoliative.

[n] includes pruritus, pruritus generalized.

Table 3 summarizes the laboratory abnormalities in REZUROCK.

Table 3: Selected Laboratory Abnormalities in Patients with Chronic GVHD Treated with REZUROCK

	REZUROCK 200 mg once daily		
	Grade 0-1 Baseline	Grade 2-4 Max Post	Grade 3-4 Max Post
Parameter	**(N)**	**(%)**	**(%)**
Chemistry			
Phosphate Decreased	76	28	7
Gamma Glutamyl Transferase Increased	47	21	11
Calcium Decreased	82	12	1
Alkaline Phosphatase Increased	80	9	0
Potassium Increased	82	7	1
Alanine Aminotransferase Increased	83	7	2
Creatinine Increased	83	4	0
Hematology			
Lymphocytes Decreased	62	29	13
Hemoglobin Decreased	79	11	1
Platelets Decreased	82	10	5
Neutrophil Count Decreased	83	8	4

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on REZUROCK

Strong CYP3A Inducers

Coadministration of REZUROCK with strong CYP3A inducers decreases belumosudil exposure *[see Clinical Pharmacology (12.3)]*, which may reduce the efficacy of REZUROCK. Increase the dosage of REZUROCK when coadministered with strong CYP3A inducers *[see Dosage and Administration (2.3)]*.

Proton Pump Inhibitors

Coadministration of REZUROCK with proton pump inhibitors decreases belumosudil exposure *[see Clinical Pharmacology (12.3)]*, which may reduce the efficacy of REZUROCK. Increase the dosage of REZUROCK when coadministered with proton pump inhibitors *[see Dosage and Administration (2.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings from animal studies and the mechanism of action *[see Clinical Pharmacology (12.1)]*, REZUROCK can cause fetal harm when administered to pregnant women. There are no available human data on REZUROCK use in pregnant women to evaluate for a drug-associated risk. In animal reproduction studies, administration of belumosudil to pregnant rats and rabbits during the period of organogenesis resulted in adverse developmental outcomes, including alterations to growth, embryo-fetal mortality, and embryo-fetal malformations at maternal exposures (AUC) approximately ≥ 3- (rat) and ≥ 0.07 (rabbit) times the human exposure (AUC) at the recommended dose (see Animal Data). Advise pregnant women and females of reproductive potential of the potential risk to the fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Animal Data

Embryo-fetal development studies were conducted in rats with administration of belumosudil to pregnant animals during the period of organogenesis at oral doses of 25, 50, 150, and 300 mg/kg/day in a pilot study and doses of 15, 50, and 150 mg/kg/day in a pivotal study. In the pilot study, maternal toxicity and embryo-fetal developmental effects were observed. Maternal toxicity (reduced body weight gain) occurred at 150 and 300 mg/kg/day doses. Increased post-implantation loss occurred at 50 and 300 mg/kg/day. Fetal-malformations were observed at ≥ 50 mg/kg/day and included absence of anus and tail, omphalocele, and dome shaped head. The exposure (AUC) at 50 mg/kg/day in rats is approximately 3 times the human exposure at the recommended dose of 200 mg.

In an embryo-fetal developmental study in rabbits, pregnant animals administered oral doses of belumosudil at 50, 125, and 225 mg/kg/day during the period of organogenesis resulted in maternal toxicity and embryo-fetal developmental effects. Maternal toxicity (body weight loss and mortality) was observed at doses ≥ 125 mg/kg/day. Embryo-fetal effects were observed at doses ≥ 50 mg/kg/day and included spontaneous abortion, increased post-implantation loss, decreased percentage of live fetuses, malformations, and decreased fetal body weight. Malformations included those in the tail (short), ribs (branched, fused or deformed), sternebrae (fused), and neural arches (fused, misaligned, and deformed). The exposure (AUC) at 50 mg/kg/day in rabbits is approximately 0.07 times the human exposure at the recommended dose of 200 mg.

8.2 Lactation

Risk Summary

There are no data available on the presence of belumosudil or its metabolites in human milk or the effects on the breastfed child, or milk production. Because of the potential for serious adverse reactions from belumosudil in the breastfed child, advise lactating women not to breastfeed during treatment with REZUROCK and for at least one week after the last dose.

8.3 Females and Males of Reproductive Potential

REZUROCK can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing

Verify the pregnancy status of females of reproductive potential prior to initiating treatment with REZUROCK.

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with REZUROCK and for at least one week after the last dose of REZUROCK. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to a fetus.

Males

Advise males with female partners of reproductive potential to use effective contraception during treatment with REZUROCK and for at least one week after the last dose of REZUROCK.

Infertility

Females

Based on findings from rats, REZUROCK may impair female fertility. The effect on fertility is reversible *[see Nonclinical Toxicology (13.1)]*.

Males

Based on findings from rats and dogs, REZUROCK may impair male fertility. The effects on fertility are reversible *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of REZUROCK have been established in pediatric patients 12 years and older. Use of REZUROCK in this age group is supported by evidence from adequate and well-controlled studies of REZUROCK in adults with additional population pharmacokinetic data demonstrating that age and body weight had no clinically meaningful effect on the pharmacokinetics of drug substance, that the exposure of drug substance is expected to be similar between adults and pediatric patients age 12 years and older, and that the course of disease is sufficiently similar in adult and pediatric patients to allow extrapolation of data in adults to pediatric patients.

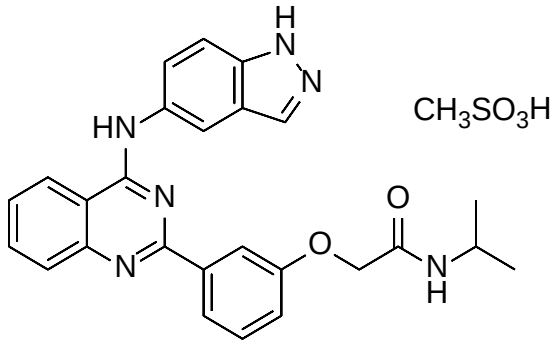
The safety and effectiveness of REZUROCK in pediatric patients less than 12 years old have not been established.

8.5 Geriatric Use

Of the 186 patients with chronic GVHD in clinical studies of REZUROCK, 26% were 65 years and older. No clinically meaningful differences in safety or effectiveness of REZUROCK were observed in comparison to younger patients.

11 DESCRIPTION

Belumosudil is a kinase inhibitor. The active pharmaceutical ingredient is belumosudil mesylate with the molecular formula $C_{27}H_{28}N_6O_5S$ and the molecular weight is 548.62 g/mol. The chemical name for belumosudil mesylate is 2-{3-[4-(1*H*-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-*N*-(propan-2-yl) acetamide methanesulfonate (1:1). The chemical structure is as follows:



Belumosudil mesylate is a yellow powder that is practically insoluble in water, slightly soluble in methanol and DMF and soluble in DMSO.

REZUROCK tablets are for oral administration. Each tablet contains 200 mg of the free base equivalent to 242.5 mg of belumosudil mesylate. The tablet also contains the following inactive ingredients: microcrystalline cellulose, hypromellose, croscarmellose sodium, colloidal silicon dioxide, and magnesium stearate.

The tablet film consists of polyvinyl alcohol, polyethylene glycol, talc, titanium dioxide and yellow iron oxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Belumosudil is an inhibitor of rho-associated, coiled-coil containing protein kinase (ROCK) which inhibits ROCK2 and ROCK1 with IC_{50} values of approximately 100 nM and 3 µM, respectively. Belumosudil down-regulated proinflammatory responses via regulation of STAT3/STAT5 phosphorylation and shifting Th17/Treg balance in ex-vivo or in vitro-human T cell assays. Belumosudil also inhibited aberrant pro-fibrotic signaling, in vitro. In vivo, belumosudil demonstrated activity in animal models of chronic GVHD.

12.2 Pharmacodynamics

Belumosudil exposure-response relationships and the time course of pharmacodynamic response are not established.

12.3 Pharmacokinetics

The following pharmacokinetic parameters are presented for chronic GVHD patients administered belumosudil 200 mg once daily, unless otherwise specified. The mean (% coefficient of variation, %CV) steady-state AUC and C_{max} of belumosudil was 22700 (48%) h•ng/mL and 2390 (44%) ng/mL, respectively. Belumosudil C_{max} and AUC increased in an approximately proportional manner over a dosage range of 200 and 400 mg (1 to 2 times once daily recommended dosage). The accumulation ratio of belumosudil was 1.4.

Absorption

Median T_{max} of belumosudil at steady state was 1.26 to 2.53 hours following administration of 200 mg once daily or twice daily in patients. The mean (%CV) bioavailability was 64% (17%) following a single belumosudil dose in healthy subjects.

Effect of Food

Belumosudil C_{max} and AUC increased 2.2 times and 2 times, respectively, following administration of a single belumosudil dose with a high-fat and high-calorie meal (800 to 1,000 calories with approximately 50% of total caloric content of the meal from fat) compared to the fasted state in healthy subjects. Median T_{max} was delayed 0.5 hours.

Distribution

The geometric mean volume of distribution after a single dose of belumosudil in healthy subjects was 184 L (geo CV% 67.7%).

Belumosudil binding to human serum albumin and human α_1-acid glycoprotein was 99.9% and 98.6%, respectively, in vitro.

Elimination

The mean (%CV) elimination half-life of belumosudil was 19 hours (39%), and clearance was 9.83 L/hours (46%) in patients.

Metabolism

Belumosudil is primarily metabolized by CYP3A4 and to a lesser extent by CYP2C8, CYP2D6, and UGT1A9, in vitro.

Excretion

Following a single oral dose of radiolabeled belumosudil in healthy subjects, 85% of radioactivity was recovered in feces (30% as unchanged) and less than 5% in urine.

Specific Populations

No clinically significant differences in belumosudil pharmacokinetics were observed with regard to age (18 to 77 years), sex, weight (38.6 to 143 kg), or mild to moderate renal impairment (eGFR $\geq$ 60 and < 90 mL/min/1.72m^2 to eGFR $\geq$ 30 and < 60 mL/min/1.72m^2). The effect of severe renal impairment on the pharmacokinetics of belumosudil has not been studied.

Drug Interaction Studies

Clinical Studies and Model-Informed Approaches

Effects of Other Drugs on Belumosudil

Strong Cytochrome P450 (CYP) 3A Inhibitors: There was no clinically meaningful effect on belumosudil exposure when coadministered with itraconazole in healthy subjects.

Strong CYP3A Inducers: Coadministration of rifampin decreased belumosudil C_{max} by 59% and AUC by 72% in healthy subjects.

Moderate CYP3A Inducers: Coadministration of efavirenz is predicted to decrease belumosudil C_{max} by 32% and AUC by 35% in healthy subjects.

Proton Pump Inhibitors: Coadministration of rabeprazole decreased belumosudil C_{max} by 87% and AUC by 80%, and omeprazole decreased belumosudil C_{max} by 68% and AUC by 47% in healthy subjects.

Effects of Belumosudil on Other Drugs

CYP3A Substrates: Coadministration of belumosudil is predicted to increase midazolam (a sensitive CYP3A substrate) C_{max} and AUC approximately 1.3- and 1.5-fold, respectively.

CYP2C9 Substrates: Coadministration of belumosudil is not expected to have clinically meaningful effect on the exposure of CYP2C9 substrates (such as warfarin).

CYP2C8 Substrates: Coadministration of belumosudil is not expected to have clinically meaningful effect on the exposure of CYP2C8 substrates that are not an OATP1B1 substrate.

In Vitro Studies

Transporter Systems: Belumosudil is a substrate of P-gp. Belumosudil inhibits BCRP, P-gp, and OATP1B1 at clinically relevant concentrations.

Enzymes Systems: Belumosudil is an inhibitor of CYP1A2, CYP2C19, CYP2D6, UGT1A1 and UGT1A9.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been conducted with belumosudil.

Belumosudil was not genotoxic in an in vitro bacterial mutagenicity (Ames) assay, in vitro chromosome aberration assay in human peripheral blood lymphocytes (HPBL) or an in vivo rat bone marrow micronucleus assay.

In a combined male and female rat fertility study, belumosudil-treated male animals were mated with untreated females, or untreated males were mated with belumosudil-treated females. Belumosudil was administered orally at doses of 50, 150 or 275 mg/kg/day to male rats 70 days prior to and throughout the mating period, and to female rats 14 days prior to mating and up to Gestation Day 7. At the dose of 275 mg/kg/day, adverse findings in female rats (treated with belumosudil or untreated but mated with treated males) included increased pre- or post-implantation loss and decreased number of viable embryos. Administration of belumosudil to male rats at a dose of 275 mg/kg/day resulted in abnormal sperm findings (reduced motility, reduced count, and increased percentage of abnormal sperm), and testes/epididymis organ changes (reduced weight and degeneration). Fertility was reduced in both treated males or females at the 275 mg/kg/day dose and reached statistical significance in males. Adverse changes in male and female reproductive organs also occurred in general toxicology studies; findings included spermatozoa degeneration at a belumosudil dose of 35 mg/kg/day in dogs and decreased follicular development in ovaries at 275 mg/kg/day in rats. Changes were partially or fully reversed during the recovery period. The exposure (AUC) at the doses of 35 mg/kg/day in dogs, and 275 mg/kg/day in rats is 0.5 times and 8-9 times, respectively, the clinical exposure at the recommended dose of 200 mg daily.

14 CLINICAL STUDIES

14.1 Chronic Graft versus Host Disease

Study KD025-213 (NCT03640481) was a randomized, open-label, multicenter study of REZUROCK for treatment of patients with chronic GVHD who had received 2 to 5 prior lines of systemic therapy and required additional treatment. Patients were excluded from the studies if platelets were < 50 × 10^9/L; absolute neutrophil count < 1.5 × 10^9/L; AST or ALT > 3 × ULN; total bilirubin > 1.5 × ULN; QTc(F) > 480 ms; eGFR < 30 mL/min/1.73 m^2; or FEV1 ≤ 39%. There were 66 patients treated with REZUROCK 200 mg taken orally once daily. Concomitant treatment with supportive care therapies for chronic GVHD was permitted. Concomitant treatment with GVHD prophylaxis and standard care systemic chronic GVHD therapies was permitted as long as the subject has been on a stable dose for at least 2 weeks prior to study. Initiation of new systemic chronic GVHD therapy while on study was not permitted.

Demographics and baseline characteristics are summarized in **Table 4**.

Table 4: Demographics and Baseline Characteristics of Patients with Chronic GVHD

	REZUROCK 200 mg once daily (N=65)
Age, Median, Years (minimum, maximum)	53 (21, 77)
Age ≥ 65 Years, n (%)	17 (26)
Male, n (%)	42 (65)
Race, n (%)	
White	54 (83)
Black	6 (9)
Other or Not Reported	5 (8)
Median (range) time (months) from Chronic GVHD Diagnosis	25.3 (1.9, 162.4)
≥ 4 Organs Involved, n (%)	31 (48)
Median (range) Number of Prior Lines of Therapy	3 (2, 6)
Number of Prior Lines of Therapy, n (%)	
2	23 (35)
3	12 (19)
4	15 (23)
≥ 5	15 (23)
Prior chronic GVHD treatment with ibrutinib, n (%)	21 (32)
Prior chronic GVHD treatment with ruxolitinib, n (%)	20 (31)
Refractory to Last Therapy, n (%[a])	43/55 (78)
Severe chronic GVHD, n (%)	46 (71)

	REZUROCK 200 mg once daily (N=65)
Median (range) Global Severity Rating	7 (2, 9)
Median (range) Lee Symptom Scale Score at baseline	27 (7, 56)
Median (range) Corticosteroid dose at baseline (PE/kg)[b]	0.19 (0.03, 0.95)

[a] Denominator excludes patients with unknown status
[b] Prednisone equivalents/kilogram

The efficacy of REZUROCK was based on overall response rate (ORR) through Cycle 7 Day 1 where overall response included complete response or partial response according to the 2014 NIH Response Criteria. The ORR results are presented in **Table 5**. The ORR was 75% (95% CI: 63, 85). The median duration of response, calculated from first response to progression, death, or new systemic therapies for chronic GVHD, was 1.9 months (95% CI: 1.2, 2.9). The median time to first response was 1.8 months (95% CI: 1.0, 1.9). In patients who achieved response, no death or new systemic therapy initiation occurred in 62% (95% CI: 46, 74) of patients for at least 12 months since response.

Table 5: Overall Response Rate through Cycle 7 Day 1 for Patients with Chronic GVHD in Study KD025-213

	REZUROCK 200 mg once daily (N=65)
Overall Response Rate (ORR)	49 (75%)
95% Confidence Interval[a]	(63%, 85%)
Complete Response	4 (6%)
Partial Response	45 (69%)

[a] Estimated using Clopper-Pearson method

ORR results were supported by exploratory analyses of patient-reported symptom bother which showed at least a 7-point decrease in the Lee Symptom Scale summary score through Cycle 7 Day 1 in 52% (95% CI: 40, 65) of patients.

16 HOW SUPPLIED/STORAGE AND HANDLING

REZUROCK 200 mg tablets are supplied as pale yellow film-coated oblong tablets containing 200 mg of belumosudil (equivalent to 242.5 mg belumosudil mesylate). Each tablet is debossed with "KDM" on one side and "200" on the other side and is packaged as follows:

200 mg tablets in 30 count bottle: NDC 79802-200-30

Store at room temperature, 20°C to 25°C (68°F to 77°F); excursions permitted from 15°C and 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Dispense to patient in original container only. Store in original container to protect from moisture. Replace cap securely each time after opening. Do not discard desiccant.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Embryo-fetal Toxicity*:*

- Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.1), Use in Specific Populations (8.1, 8.3)]*.
- Advise females of reproductive potential to use effective contraceptive during treatment with REZUROCK and for at least one week after the last dose *[see Warnings and Precautions (5.1)]*.
- Advise males with female partners of reproductive potential to use effective contraceptive during treatment with REZUROCK and for at least one week after the last dose *[see Use in Specific Populations (8.3)]*.

Lactation

- Advise women not to breastfeed during treatment with REZUROCK and for at least one week after the last dose *[see Use in Specific Populations (8.2)]*.

Infertility

- Advise males and females of reproductive potential that REZUROCK may impair fertility *[see Use in Specific Populations (8.3)]*.

Administration

- Inform patients to take REZUROCK orally once daily with food according to their physician's instructions and that the oral dosage (tablets) should be swallowed whole with a glass of water without cutting, crushing or chewing the tablets approximately the same time each day *[see Dosage and Administration (2.1)]*.
- Advise patients that in the event of a missed daily dose of REZUROCK, it should be taken as soon as possible on the same day with a return to the normal schedule the following day. Patients should not take extra doses to make up the missed dose *[see Dosage and Administration (2.1)]*.

Drug Interactions

- Advise patients to inform their health care providers of all concomitant medications, including prescription medicines, over-the-counter drugs, vitamins, and herbal products *[see Drug Interactions (7)]*.

Active ingredient made in India.

Distributed and marketed by:

Kadmon Pharmaceuticals, LLC
Warrendale, PA 15086
1-877-377-7862

PATIENT INFORMATION
REZUROCK (REZ-ur-ok)
(belumosudil)
tablets

What is REZUROCK?

REZUROCK is a prescription medicine used to treat adults and children 12 years of age and older with chronic graft-versus-host disease (chronic GVHD) after you have received at least 2 prior treatments (systemic therapy) and they did not work.

It is not known if REZUROCK is safe and effective in children less than 12 years old.

Before taking REZUROCK, tell your healthcare provider about all of your medical conditions, including if you:

- have kidney or liver problems.
- are pregnant or plan to become pregnant. REZUROCK can harm your unborn baby. If you are able to become pregnant, your healthcare provider will do a pregnancy test before starting treatment with REZUROCK. Tell your healthcare provider if you become pregnant or think you may be pregnant during treatment with REZUROCK.
  - **Females** who can become pregnant should use effective birth control during treatment with REZUROCK and for at least 1 week after the last dose.
  - **Males** with female partners who can become pregnant should use effective birth control during treatment with REZUROCK and for at least 1 week after the last dose.
- are breastfeeding or plan to breastfeed. It is not known if REZUROCK passes into breast milk. Do not breastfeed during treatment with REZUROCK and for at least 1 week after the last dose.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. REZUROCK may affect the way other medicines work, and other medicines may affect the way REZUROCK works.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take REZUROCK?

- Take REZUROCK exactly as your healthcare provider tells you to take it.
- Do not change your dose or stop taking REZUROCK without first talking to your healthcare provider.
- Take REZUROCK 1 time a day with a meal.
- Take REZUROCK at about the same time each day.
- Swallow REZUROCK tablets whole with a glass of water.
- Do not cut, crush, or chew REZUROCK tablets.
- Your healthcare provider will do blood tests to check your liver at least 1 time a month during treatment with REZUROCK.
- If you miss a dose of REZUROCK, take it as soon as you remember on the same day. Take your next dose of REZUROCK at your regular time on the next day. Do not take extra doses of REZUROCK to make up for a missed dose.
- If you take too much REZUROCK, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of REZUROCK?

The most common side effects of REZUROCK include:

- infections
- tiredness or weakness
- nausea
- diarrhea
- shortness of breath
- cough
- swelling
- bleeding
- stomach (abdominal) pain
- muscle or bone pain
- headache
- high blood pressure

Your healthcare provider may change your dose of REZUROCK, temporarily stop, or permanently stop treatment with REZUROCK if you have certain side effects.

REZUROCK may affect fertility in males and females. Talk to your healthcare provider if this is a concern for you.

These are not all the possible side effects of REZUROCK.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Kadmon Pharmaceuticals, LLC at 1-877-377-7862.

How should I store REZUROCK?

- Store REZUROCK at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep REZUROCK in its original container. The REZUROCK bottle contains a desiccant packet to help keep your tablets dry (protect from moisture). Keep the desiccant in the bottle.

- Tightly close the REZUROCK bottle after you take your dose.

Keep REZUROCK and all medicines out of the reach of children.

General information about the safe and effective use of REZUROCK.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use REZUROCK for a condition for which it was not prescribed. Do not give REZUROCK to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about REZUROCK that is written for health professionals.

What are the ingredients in REZUROCK?

Active ingredient: belumosudil mesylate

Inactive ingredients:

Tablet core: microcrystalline cellulose, hypromellose, croscarmellose sodium, colloidal silicon dioxide, and magnesium stearate.

Tablet coating: polyvinyl alcohol, polyethylene glycol, talc, titanium dioxide and yellow iron oxide.

Distributed and marketed by **Kadmon Pharmaceuticals, LLC**, Warrendale, PA 15086

For more information, call 1-877-377-7862 or go to www.REZUROCK.com.

This Patient Information has been approved by the U.S. Food and Drug Administration Issued: July 2021